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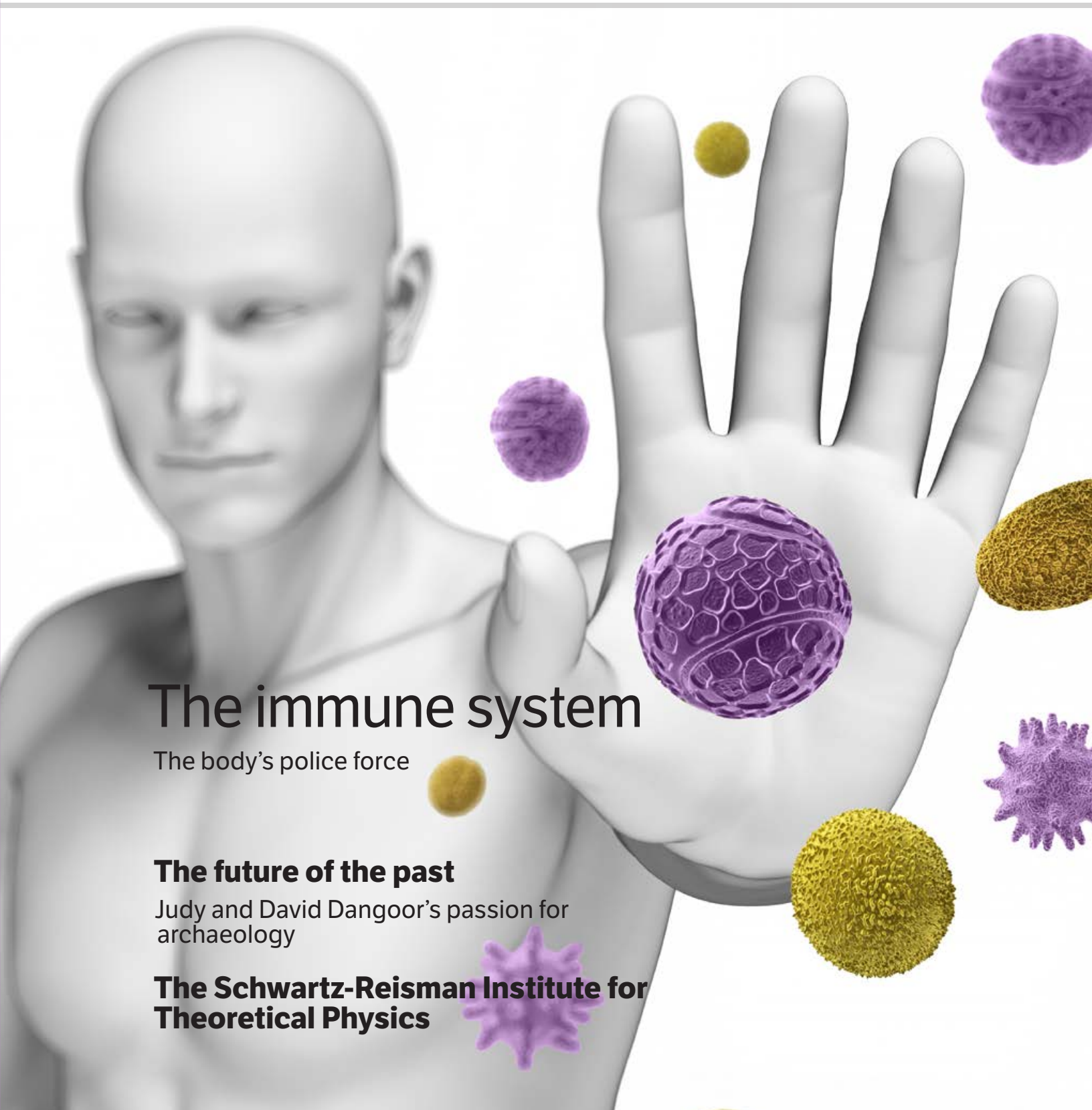

## The immune system

The body's police force

## The future of the past

Judy and David Dangoor's passion for archaeology

## The Schwartz-Reisman Institute for Theoretical Physics


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A publication of the Department of Resource Development

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# From the President

Dear Friends,

When the *New York Times* recently ran an in-depth series of articles about the promise of immunotherapy, we were not surprised. After all, immunotherapy has been the focus of keen scientific interest here at the Weizmann Institute for years, with some of the world's most important immunotherapy-related discoveries emerging from our labs, both historically and right up to the present day. In fact, it was our recognition of the dynamism of the field that inspired us to choose the topic of this magazine's cover story: an overview of the Weizmann Institute's contribution to both immunology research and breakthroughs in immunotherapy for cancer.

When Prof. Zelig Eshhar of the Institute's Department of Immunology began exploring how genetic modification of immune cells could cause such cells to seek out and destroy cancer back in the 1980s, he was in the company of just a few other scientists worldwide convinced of cancer immunotherapy's potential. Today this hoped-for potential is "settled science" and Prof. Eshhar's T-cell research, which is now the basis for a successful drug therapy for leukemia, is just the latest success from our renowned scientists working in immunotherapy-related topics—a group that includes Prof. Michael Sela, Prof. Ruth Arnon, and others.

One of the stories to which I'd like to draw your attention describes the establishment of the Schwartz-Reisman Institute for Theoretical Physics. This new entity joins a handful of other such institutes in other places in the world. The ITP will help solidify our role as a world leader in the theoretical research that is having an impact on a huge range of academic and practical fields.

I believe our entire global community shines through on these pages, from our successful alumni to our dynamic students, to the donors that make this place "go", to the new recruits and veteran scientists who, together, are maintaining the Institute's worldwide reputation as a center of great science for the benefit of all humanity.

With best wishes for a happy and healthy New Year,
**Prof. Daniel Zajfman**
President, Weizmann Institute of Science

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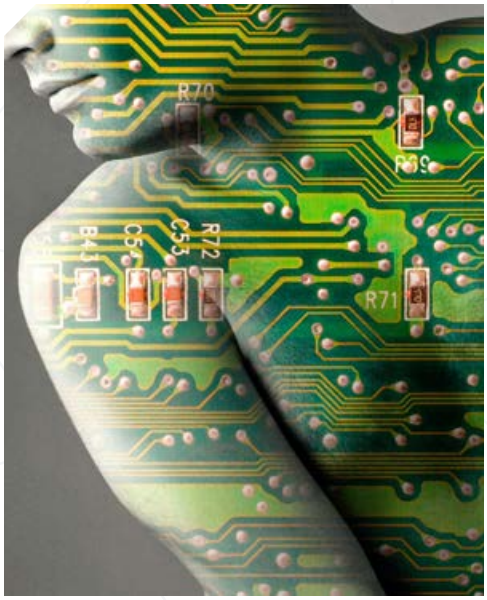

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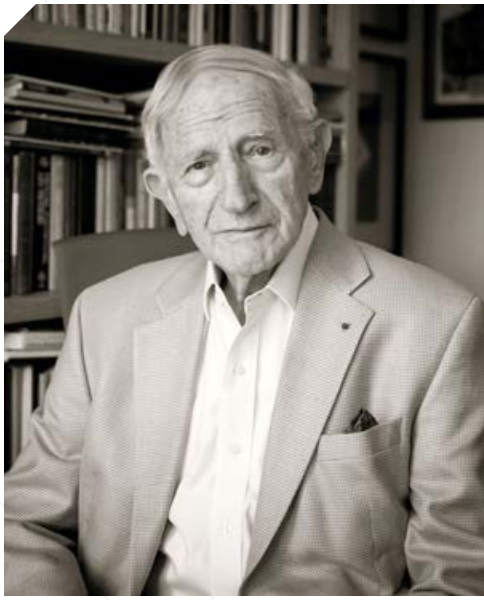

*Cover story*

**22 Prof. Michael Sela**

# Stress in the brain

Two recent studies by Prof. Alon Chen, head of the Department of Neurobiology, have shown how the management of stress is built into our brains.

## A "switch" for social stress

As reported recently in *Nature Neuroscience*, Prof. Chen showed how people who make friends easily may be hard-wired to do so, thanks to a neural mechanism that—when switched on—regulates one's ability to cope with social challenges.

The mechanism involves a small signaling molecule called Urocortin-3, and a receptor on the surface of neurons to which Urocortin-3 binds. Drs. Yair Shemesh and Oren Forkosh—both members of Prof. Chen's lab—found that varying levels of Urocortin-3 may help determine how willing we are to leave the safety of our social group and strike up new relationships.

The researchers devised a "social maze" for mice that allowed them to choose whether to interact with familiar mice or with strangers, or to avoid social contact altogether. They also designed a special arena in which group interactions could be tracked with video cameras.

Prof. Alon Chen

Prof. Alon's team demonstrated how mice with high levels of Urocortin-3 in the brain actively sought out contacts with new, unfamiliar mice. But when this receptor was blocked, the mice chose to socialize mainly within the most familiar group, and to avoid strangers.This stress-regulation mechanism may impart an evolutionary advantage, says Prof. Chen, stimulating social contact within trusted groups, while promoting caution with intruders. And, he adds, what's true of mice may be true of men.

"Since an analogous system operates in the human brain, our findings suggest that this mechanism might be responsible for coping with social stress," he says. "Disruption of this mechanism may be implicated in social anxiety, as well as more serious behavioral disorders."

## Food-related stress: hard-wired in women?

Research suggests that of those struggling with serious eating disorders such as anorexia and bulimia, only about 10 percent are male. While many blame cultural messages that strongly link female thinness with social acceptability, this gender discrepancy may be based, at least in part, on differences between the male and female brain.

A study by Dr. Yael Kuperman, a staff scientist in the Department of Veterinary Resources has demonstrated a critical difference in how the male and female brains react to stressful situations. Working with graduate student Meira Weiss, Dr. Kuperman began this study while still a doctoral student in Prof. Chen's lab.

The team discovered that, in about half the neurons known to be involved in the arousal of appetite, a receptor called CRFR1 mediates the body's stress response. To investigate the exact role of CRFR1, the researchers created a mouse model in which this receptor was removed specifically from these appetite-associated cells. The mice were then monitored for their response to stressful stimuli, including the withholding of food. When the mice were exposed to stressful stimuli, the female CRFR1-deficient mice displayed a dramatic reaction—the level of glucose produced by their livers dropped significantly—while the male mice were barely affected.

The findings show that male and female bodies exhibit significant differences in their metabolic response to stressful challenges. They may also help explain why women are much more prone to eating disorders than men—a discovery that could lead to the development of drugs that mediate behaviors associated with eating disorders.

# Science Briefs

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## A new weapon in the battle against antibiotic resistance

*Prof. Rotem Sorek, who used bacteria from his own lab members' teeth to detect antibiotic-resistance genes.*

Antibiotics are a class of drugs that treat bacterial infections by stopping growth of bacteria or killing the bacteria directly. But as Alexander Fleming, discoverer of penicillin, noted in his Nobel Prize acceptance speech, even the best antibiotics can become ineffective over time. With improper prescribing of antibiotic medication triggering selective survival of resistant strains, resistance is a growing worldwide problem.

It's a problem that many scientists have been working to solve. The Weizmann Institute's Prof. Ada Yonath of the Department of Structural Biology was awarded the Nobel Prize for her mapping of the ribosome, the cell's protein factory. Her discovery has major implications for solving antibiotic resistance, because certain antibiotics eliminate pathogenic bacteria by binding to ribosomes, preventing them from producing crucial proteins.

Now, Institute scientists have created a new method for identifying the molecular mechanisms that allow bacteria to thrive, even in the presence of therapeutic levels of medication.

Prof. Rotem Sorek of the Department of Molecular Genetics has developed a high-throughput approach to the discovery of factors that regulate bacterial gene expression—specifically, those genes that, in their active state, contribute to antibiotic resistance. His findings were published in *Science* in April.

Prof. Sorek looked at riboregulators—RNA elements that, in the presence of specific molecules, trigger the premature termination of protein production. "We found a way to identify riboregulators on the genome-wide scale in a living cell. We can measure the activity of many of these riboregulators in parallel, and we can screen for ones that respond to antibiotics." Using this method, his team detected a number of riboregulators that control the activation of genes involved in antibiotic resistance. These findings allowed them to identify not only known, but also novel, genes involved—results which may lead to new therapeutic strategies.

So far, Prof. Sorek has used the platform to detect numerous factors involved in the regulation of antibiotic-resistance genes, both in pathogenic bacteria and in bacteria collected from a much friendlier source—his own lab members' teeth. He believes that he and his colleagues will continue to smile—and not just in order to provide additional bacterial samples. "Our approach opens the door to identifying the genes used by bacteria to resist antibiotics. We hope to develop means to inhibit these genes, so that antibiotic medications can do their job."

# Virus in fetal brain can lead to schizophrenia, autism

A dire phenomenon observed many years ago was later confirmed in scientific studies: When women were infected by a particular virus called cytomegalovirus (CMV) during pregnancy, it affected the developing baby's brain. When the infection occurred early in pregnancy, it increased the likelihood that offspring would later be diagnosed with autism. When the infection occurred closer to the time of birth, such women gave birth to children who, later in life, had an increased risk of schizophrenia.

Now, Weizmann Institute researchers have identified a molecular mechanism—rooted in the immune cells of the developing fetal brain—that helps explain how CMV infection during pregnancy can increase the incidence of these neurodevelopmental diseases, and also explains how infection at different stages of pregnancy can promote different disease outcomes. The study was published in *Science* in June.

Prof. Michal Schwartz and Dr. Ido Amit, of the departments of Neurobiology and Immunology, respectively, and their lab teams examined microglia—the sole type of immune cells present in the brain. They determined that an immune response triggered by CMV infection can cause early-stage microglia cells to mature too early—disrupting normal brain development, and leading to malfunction.

The scientists discovered that, in the brain, normal immune cell development occurs in three distinct stages: early-stage cells that populate the embryo's brain, pre-microglia cells, and adult cells. The second stage is the most sensitive to disruption. This is because, close to birth and shortly afterwards, pre-microglia cells perform important brain-stabilizing tasks including siphoning off superfluous neuronal networks and strengthening connections between neurons.

*Prof. Michal Schwartz*

Infection by CMV during late pregnancy triggers the rapid transformation of the pre-microglia population into mature immune cells capable of mounting an anti-viral response.

*Dr. Ido Amit*

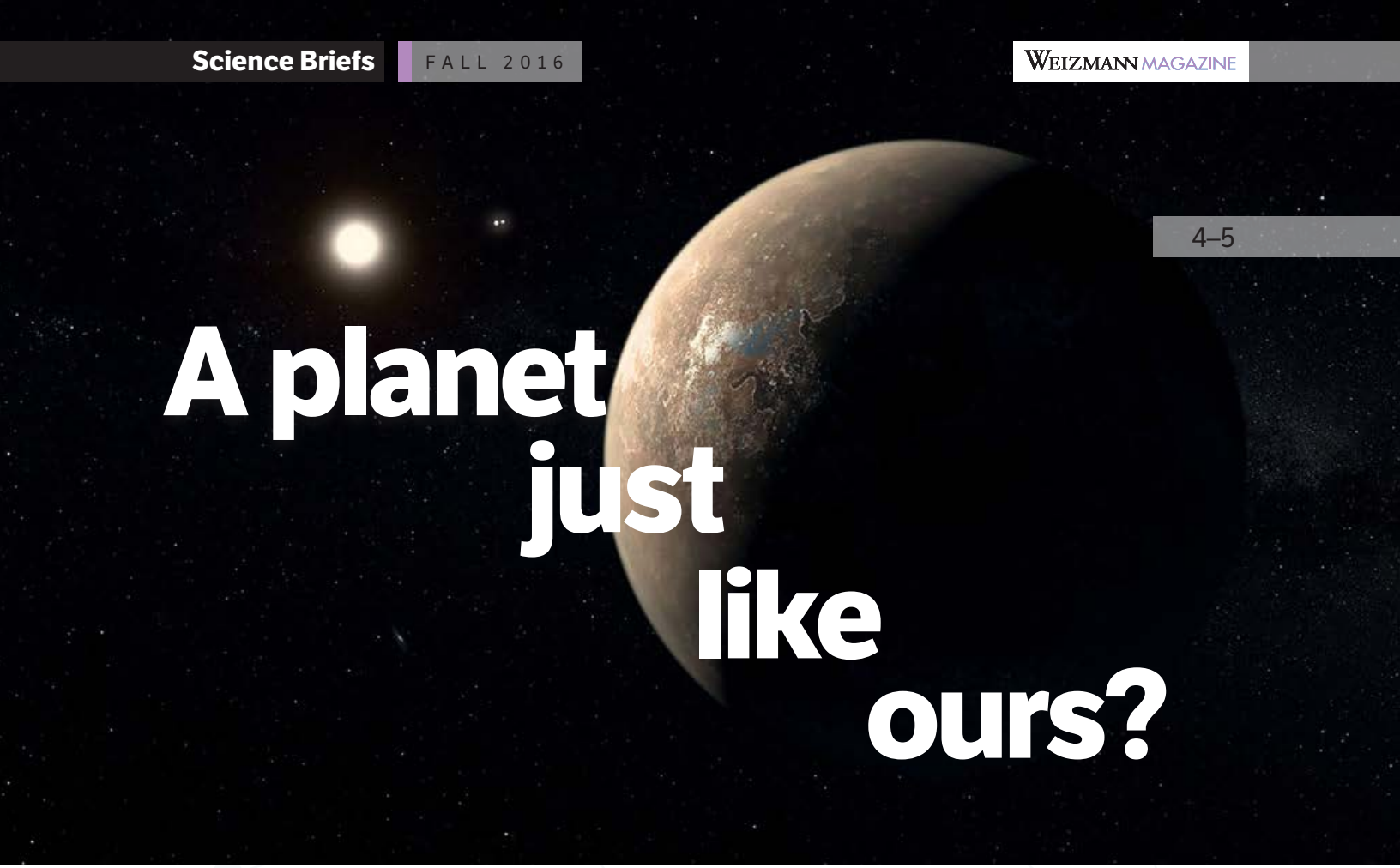
This reduces the availability of the right form of microglia at a critical time during brain development—the form needed to stabilize and "edit" developing neural networks. According to Prof. Schwartz, this deviation from the normal schedule can mark the tipping point between healthy offspring and offspring that will develop neurodevelopmental disease.

"The offspring of moms who had been exposed to materials mimicking CMV infection during pregnancy exhibited abnormal behavior, including disturbances in social interaction and behaviors similar to those of people with schizophrenia," Prof. Schwartz says. "This indicates that it's essential for the development of immune cells in the brain to be synchronized with the development of the brain itself."

Dr. Amit adds: "Because microglia development proceeds in three stages, disrupting this process at different points has different results. "When infection throws the normal transition between the second and third stage off-schedule, the result can be schizophrenia. When it occurs earlier, the result may be autism."

Orit Matcovitch-Natan, a graduate student in the Schwartz and Amit labs and the study's lead author, adds: "This research paves the way for studying the effects of other viruses on the mother's immune system and helps elucidate the connection between immunity and neurodevelopmental disorders."

# A planet just like ours?



*An artist's rendering of Proxima Centauri b*

An international astronomy team announced in August that a planet with a mass similar to that of Earth has been observed orbiting the star Proxima Centauri b, the closest star to our Sun, just over four light years (about 40 trillion km) away. The collaboration of scientists from nine countries, known as the "Pale Red Dot" and led by Dr. Guillem Anglada-Escudé of the Queen Mary University of London, included the Weizmann Institute of Science's Dr. Aviv Ofir in the group of Prof. Oded Aharonson of the Department of Earth and Planetary Sciences.

Proxima Centauri b is a red dwarf—a star with a diameter about one-seventh that of our Sun and much dimmer; it gives off only ⅙₀₀ the light of the Sun. The team's calculations show that the planet has a mass of at least 1.3 times that of Earth, and its year—the time it takes to orbit its sun—is a little over 11 days.

It orbits very close to its sun—only 5 percent of the distance from Earth to our Sun—but since its sun is so dim, the temperatures on Proxima Centauri b may be relatively balmy, and liquid water could theoretically exist on its surface. The range of distances where the planet's temperature permits liquid water is often referred to as "the habitable zone."

Dr. Ofir says that it is not at all clear whether life as we know it could have evolved on the planet, and the subject is already the focus of intense debate.

The planet was discovered through measurements of the radial velocity of the star. Such measurements rely on the Doppler effect—the shift in wavelength as an object moves closer or away from the viewer. According to the team's measurements, the star is moving at a speed of about a meter per second (or 3.6 km/h) towards and away from us.

Proxima Centauri has been studied for the past century, but only now have observations become sensitive enough to decisively detect the presence of this small planet. "We discovered the planet with an observatory in Chile. We can't see Proxima Centauri from our observatories in Israel. It is well below the southern horizon, so it is unobservable from Israel all year round."

All criminals have their sidekicks who help them carry out their bad deeds. Cancer cells grow and replicate in much the same way—with the assistance of their surrounding environment.

This so-called "tumor microenvironment" is receiving increasing attention from the global community of research scientists. One of the new, young leaders in this field is Dr. Ruth Scherz-Shouval, who joined the Weizmann Institute in 2015 after a postdoctoral fellowship at the Massachusetts Institute of Technology (MIT).

The question she is pursuing is how cancer cells recruit and subvert normal cells to create an environment that promotes tumor progression and metastasis. What is known, so far, is that cancer cells activate normal, surrounding cells to form blood vessels and connective tissue that fight the immune system. She wants to know, specifically, which mechanisms are at work throughout this process.

Dr. Scherz-Shouval did her PhD at the Weizmann Institute under the guidance of Prof. Zvulun Elazar, an expert in the process of autophagy—the ability of the body's cells to discard or recycle defective or toxic materials. She made a major contribution to the field by unraveling a novel mechanism of regulation of autophagy, mediated by reactive oxygen species such as hydrogen peroxide. Then she did a first postdoctoral fellowship with Prof. Moshe Oren, an expert in cancer research who directs the Moross Integrated Cancer Center.

For her second postdoc, at the Whitehead Institute for Biomedical Research at MIT, she received a grant from the Israel National Program for Advancing Women in Science that is led by the Weizmann Institute. The grant, given to 10 outstanding

# New Scientists

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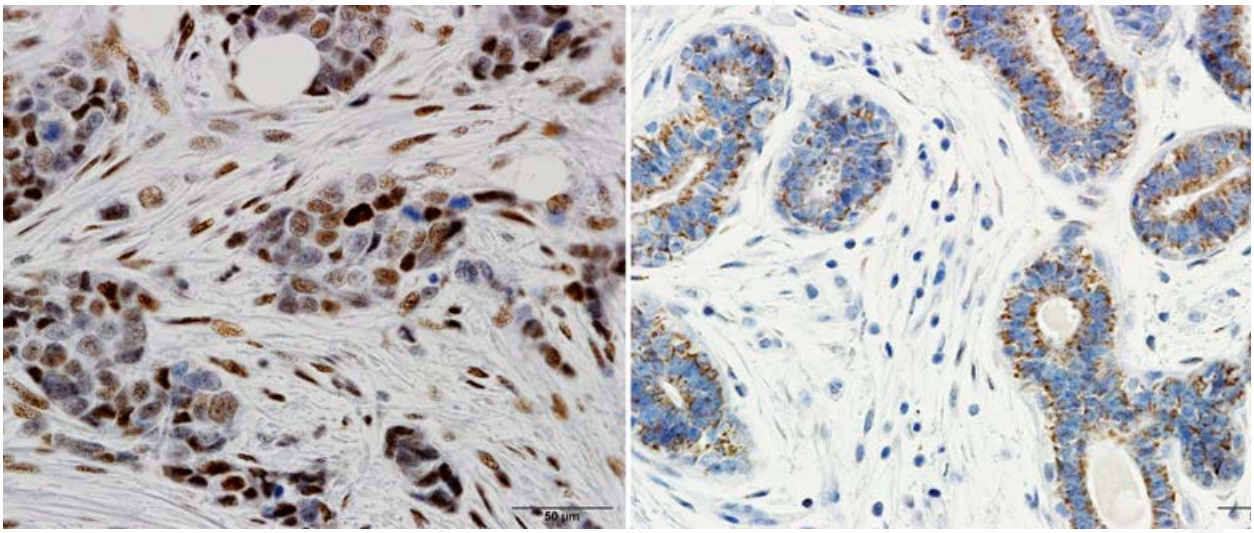
# Dr. Ruth Scherz-Shouval

## Investigating cancer's partners in crime: the microenvironment



*Tissue from a human breast showing tumor cells with activated heat shock factor 1 stained brown and normal cells shown in blue. This illustrates that tumor cells need HSF1 in order to continue thriving.*

women scientists per year to conduct postdoctoral studies abroad, is given in addition to postdoc salaries and is meant to help women and their families manage with the financial pressures typical of a postdoctoral period. In addition, she received a Human Frontier Science Program Fellowship and a Fulbright award.

With the understanding that tumors are complex organs that are highly dependent on normal cells in their environment, at MIT she set out to study the tumor microenvironment. She zeroed in on the heat shock response that cells activate when subject to thermal stress such as fever following inflammation, and identified a new role for the "master regulator" of this response, heat-shock factor 1 (HSF1), in the tumor microenvironment. She showed how HSF1 helps reprogram fibroblasts, the cells responsible for making the extracellular matrix and collagen in a tumor's nearby tissues, causing them to support the tumor's malignancy.

In collaboration with clinicians at the Brigham and Women's Hospital and Beth Israel Hospital in Boston, and Rabin Medical Center in Israel, clinical studies confirmed that in early-stage breast and lung cancer, high stromal HSF1 activation is strongly associated with poor patient outcome, a finding that has significant diagnostic and therapeutic implications. Her research may also have implications for inflammation more generally, in particular inflammatory bowel disease (IBD).

In her new lab at the Institute, she is broadening her work on how stress responses rewire and reshape the tumor microenvironment, creating a tumor-supportive environment that drives cancer progression and metastasis.

# Nature vs. nurture

*First Zuckerman Scholar Dr. Ivo Spiegel is exploring the age-old question in a whole new way*

*Dr. Spiegel identified a number of so-called "secreted growth factors" that are expressed in subsets of cortical neurons when a person has a sensory experience.*



To what extent do experience and environment dictate brain function, and to what extent do our genes do so? It is a question many have been asking for decades. Dr. Ivo Spiegel, a new recruit to the Department of Neurobiology, is tackling this quandary in a highly creative way. His work has implications for a variety of disorders including autism, schizophrenia, and neurodegenerative disease.

The cortex, a brain area responsible for sensory processing and memory storage, is home to a diverse population of neurons, each with its own distinct function. Excitatory neurons receive electric input and generate a stimulating output for connected neurons. Inhibitory neurons do the exact opposite: They transmit to their connected neurons a signal that is inhibitory as it opposes the currents coming from the excitatory neurons. Thus, whether a given neuron will or will not send an electric signal to the next neuron is determined by the amount of excitation and inhibition that it receives.

The tight control over this balance between the amounts of excitation and inhibition (E/I balance) in the face of changing sensory experiences is critically important for normal brain function. It is achieved by regulating the synapses—the sites through which neurons connect to each other. Genetic mutations that affect synapses and lead to changes in E/I balance were recently linked to psychiatric disorders such as autism and schizophrenia.

Dr. Spiegel's work focuses on E/I balance. He is making key inroads into understanding how this dynamic is affected by both genes and environmental factors, while revealing new data about the impact E/I balance has on brain function in both health and disease.

He received his BSc in biology with honors from Tel Aviv University, and then moved to the Weizmann Institute, where he received his MSc in 2001 and his PhD in 2007.

During his postdoctoral training at Harvard Medical School, he began to explore the molecular components underlying this delicate balancing mechanism and its effect on brain function and health. He identified a feature (a so-called "transcriptional program") embedded in the genome that regulates the amount of excitation and inhibition impinging onto a given neuron—and thus helps maintain normal brain function. Each type of neuron responds to sensory stimulation by activating a unique transcriptional program, which modifies the synapses onto this neuron, thereby affecting the function of the circuit.

Dr. Spiegel also identified a number of so-called "secreted growth factors" that are expressed in subsets of cortical neurons when a person has a sensory experience. These growth factors, he found, play a role in regulating specific sets of synapses and thereby mediating the adaptation of neural circuits to experience.

He is the first Zuckerman Scholar to join the Weizmann Institute as a new tenure-track scientist. The Zuckerman STEM Leadership Program was kicked off last January with a gift of $100 million from American business leader and philanthropist Mortimer B. Zuckerman, with a goal to cultivate deeper scientific ties between North America and Israel. The gift, which is split evenly between four Israeli institutions of higher learning including the Weizmann Institute, funds postdoctoral fellows from the U.S., Canada, and other Western countries during their fellowship periods in Israel. It also supports the recruitment of top Israeli scholars like Dr. Spiegel from abroad who join the faculties of the Israeli institutions, enabling the Israeli institutions to effectively compete with top North American institutions for the best candidates.

The other participating institutions are the Technion-Israel Institute of Technology, Tel Aviv University, and The Hebrew University of Jerusalem.

In his new lab at the Weizmann Institute, Dr. Spiegel will continue to investigate the inner mechanics underlying the E/I balance. In this way, he hopes to identify the mechanisms responsible for various psychiatric diseases and how our internal, emotional states regulate brain function.

# The future of the past

*Judy and David Dangoor are ensuring science informs our past and better secures our future*

# Spotlight On

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## Archaeology isn't what it used to be anymore.

In their work learning about key events in time and refining the chronological record, archaeologists have relied mainly on a keen and educated eye to elucidate past events and place them in time. Today, however, a new brand of archaeology—one that integrates scientific analysis, including tools from chemistry, physics and biology, with traditional techniques—is emerging, and Weizmann Institute scientists are leading the way.

Advanced infrastructure is a key factor in propelling Weizmann Institute scientists' study of the past into the future. Particularly important is a relatively new piece of equipment called the Dangoor-Research Accelerator Mass Spectrometer (D-REAMS). Inaugurated in 2013, the D-REAMS Laboratory was made possible thanks to a major gift by Dr. Judy and David Dangoor of London and the Exilarch's Foundation, established by David's father, Sir Naim Dangoor. The D-REAMS Lab is headed by Dr. Elisabetta Boaretto and is already leading to discoveries that were never before possible. While many AMS laboratories exist elsewhere in the world, D-REAMS is the first AMS laboratory in the world to be used only for research rather than acting as a service provider. The technology leverages the unique science-based approach pioneered by Weizmann Institute scientists during excavation and has resulted in numerous key findings and increasingly precise dating (see sidebar, p.14).

"For us, helping establish D-REAMS was the perfect opportunity to deepen our commitment to preserving historical narrative and at the same time helping advance scientific research," says David Dangoor. "Archaeology is not an area where scientific rigor has been applied for the most

*Dr. Judy and David Dangoor at the Global Gathering in London in June*

part, but the Weizmann Institute is helping change that by doing evidence-based research—using the scientific method of trying to disprove a theory rather than trying to assert a theory, which is the way archaeological research is often done."

It was a perfect fusion of history and science, two areas that they personify: Judy Dangoor is a scientist by training—she obtained a PhD in photosynthesis at Imperial College—and David's family has been deeply involved in ensuring the preservation of the historical narrative of the Jews of Iraq, where he lived himself and attended primary school until moving to the UK in 1960.

The Dangoors first came to know the Weizmann Institute in 2009, when a professor Judy knows from her time at Imperial College asked the couple to sponsor a dinner for Making Connections, the Weizmann UK program that funds collaborations between Weizmann Institute scientists and peers at UK research institutions. The focus of the collaboration, and the topic that evening, was artificial photosynthesis. They were seated next to Weizmann Institute President Prof. Daniel Zajfman, and the friendship was off to a start.

## Sealed in history

At age eight in Baghdad, David began a stamp collection by ordering a batch from abroad. After excitedly receiving the package in the mail, he came across a stamp from a country he'd never heard of: Israel. He asked his father what it was. David recalls, "He asked me, 'Where did you get this?' and I told him. He asked me to give it to him and told me not to talk about it... That indicates the extent to which adults had to shield the Jewish children in Iraq from the politics, anti-Semitism, and anti-Israel sentiment." Two years later, when David was 10, the family moved to London.

The Dangoors were a prominent family in Baghdad at a time when Jews comprised 40 percent of the city's population. David's grandfather, Eliahou, was the largest printer of Arabic books in Iraq. His great-grandfather, Hakham Ezra Reuben Dangoor, was Baghdad's chief rabbi. Naim owned multiple businesses and the Iraqi franchise for Coca-Cola. When the majority of Jews left Iraq for the nascent state of Israel between 1949 and 1952, the Dangoors stayed; they had too much to lose. But eventually Naim brought his family to the UK and when the Ba'ath Party passed a law in 1963 placing major business restrictions on Jews, he also left. It meant leaving all his assets behind.

"My father was 50 years old when he arrived in London, and he had to start from scratch," says David. "He rebuilt, together with us, his four sons. My father was forever grateful to England for allowing us the opportunity to rebuild. And this gratiutude became the source of his philanthropy."

Until his death in 2015 at age 101, Naim Dangoor was a leader of the Iraqi Jewish community in the UK and, among other initiatives, he worked to preserve the historical narrative of the Iraqi Jewish community through his prolific writing and publication of *The Scribe*, a periodical about the Iraqi Jewish community. He started the Exilarch's Foundation, which has given generously to a multitude of causes and which David and his brothers now oversee, including 4,000 scholarships for undergraduate students studying science and technology in the UK.

The Exilarch Foundation is the largest private supporter of the Francis Crick Institute, a new biomedical research institution in London, and David and Judy support a variety of other UK causes, including Westminster Academy in London, where many of the students are immigrants from Muslim countries.

In Israel, the Foundation established the Sir Dr. Naim Dangoor Program for Universal Monotheism at Bar-Ilan University during Naim's lifetime, and it made a major gift recently to establish the Dangoor Centre for Personalised Medicine, part of Bar-Ilan University's medical school in Tzfat, which was inaugurated earlier this year. They also support the annual Anglo-Israel Cardiology Symposium, which brings together cardiologists from the UK and Israel.

As frequent visitors to Israel, they now have a house in Herzliya. They have four children and four grandchildren. "With six trips to Israel last year alone, it was about time to fulfill our dream of having a house in Israel," says David.

***It was a perfect fusion of history and science, two areas that the Dangoors personify.***

## Spreading the word

The Dangoors have since become committed to another aspect of science: communicating its relevance and importance to the public. For this reason, they stepped forward as the lead sponsors of the Institute's Global Gathering that took place in London in early June. "The Global Gathering is a chance for people in the UK to see what the Weizmann Institute is all about," says David. "The Weizmann Institute is a fantastic brand and it should get maximum exposure, and the Global Gathering reflects a drive by the Institute to share what it is doing with others. That's a wonderful quality. Moreover, the UK is where the Weizmann started, with the Sieff, Wolfson, and Clore families. To be associated with these families makes us very proud."

Adds Judy: "Science knows no boundaries; it is a collaborative effort across all peoples and persuasions. We feel it is very important to engage non-scientists with science... Israel should be supremely proud of Weizmann and its other research institutions because they have made major contributions. Let's let the world know."

# Digging deep: archaeology in the modern age

Archaeology is about the reconstruction of past human behavior based on the materials that have withstood the ravages of time. The Weizmann Institute has the advantage of being located in an area with a copious archaeological record. After all, Israel sits at the crossroads between Africa, Europe, and Asia and it was in this narrow strip between sea and desert that hominids first came out of Africa more than a million years ago, gathered into villages 14,000 years ago, and developed agriculture 10,000 years ago.

Prof. Stephen Weiner of the Department of Structural Biology was an early leader in the field that he dubbed "microarchaeology"—the elucidation of the microscopic record of artifacts using scientific tools. He advanced an integrated approach that starts at the excavation itself using an on-site laboratory. This work has been enabled by the Weizmann Institute-Max Planck Society Center for Integrative Archaeology and Anthropology, which Prof. Weiner co-directs, and the Helen and Martin Kimmel Center for Archaeological Science, which he heads.

## A new era in research

Until the establishment of the D-REAMS Lab, Dr. Elisabetta Boaretto of the Scientific Archaeology Unit—who integrates the microarchaeological approach into her own research program in archaeological science—had to send samples abroad for radiocarbon dating; the results would often take many months to arrive, inhibiting the pace of research. "Now, we can take samples straight from

*Dr. Elisabetta Boaretto*



*Prof. Steve Weiner in the field*

the field, where we know exactly where they come from, into the lab, and have results in days," says Dr. Boaretto.

Radiocarbon techniques allow archaeologists to date samples going back to 10,000 years ago with a precision range of about 50 years. The AMS technology enables more precise dating going back 50,000 years and also makes it possible to measure the amount of radiocarbon in a milligram or so of sample. This is extraordinary, because for every radiocarbon atom in a given sample there are around a trillion regular carbon atoms.

"In other words," says Dr. Boaretto, "this is like making a pile of white paper from the Earth to the moon with only one colored paper in it, and the machine will find the colored paper."

The D-REAMS machine opens up enormous possibilities for documenting the spread of new materials and technologies and reconstructing trade routes. Her team has made several important discoveries since the machine's installation:

- Precise dating of the transition from Neanderthals to modern humans about 47,000 years ago, based on charcoal fragments from sediments from the Kebara Cave near Haifa.
- The dating of the end of the city-states in the Levant at the end of the Early Bronze Age to 2500 years BCE—about 300 years earlier than was previously estimated.
- Dating of the transition of the Late Bronze Age to the Iron Age (the arrival of the Sea Peoples, including the Philistines) to the 13th century BCE, from the sites of Qubur el Walaydah and Tel es Safi.
- The earliest domestication of the fava bean, showing it occurred as early as the 11th millennium BP, which contributes to our understanding of the development of agriculture.

Says Dr. Boaretto: "The AMS machine opens up many new research opportunities for us to investigate, for example how olive trees, an important component of the local archaeological record, could be a valuable archive for past climate. Such questions require the integration of science and archaeology, and all this starts in the field and progresses to the laboratory. This approach attracts the best scientists, postdocs, and students—people who want to come to Israel to do archaeological research, and who are well trained in the natural sciences and archaeology. We can now say to them: 'You will have all the most sophisticated tools at your fingertips to do your research at the highest level.'"

"Archaeology is a subject that is common to all of the Middle East. For us, it is an opportunity for nonpolitical cooperation," says David Dangoor, adding that the cooperation with Max Planck adds another positive dimension because the Dangoors are major advocates of nourishing cooperation between Israeli scientists and scientists from other countries.

"Understanding of the past throws a lot of light on the present," says Judy Dangoor. "D-REAMS introduces the potential to develop a rigorous chronology of historical eras. I'm always fascinated with how and when and why humans moved out of Africa and the fact that the rest of the world population ostensibly is derived from that group. And it wasn't so long ago. It is very sobering how we're all very much connected to each other."

# A force to be reckoned with

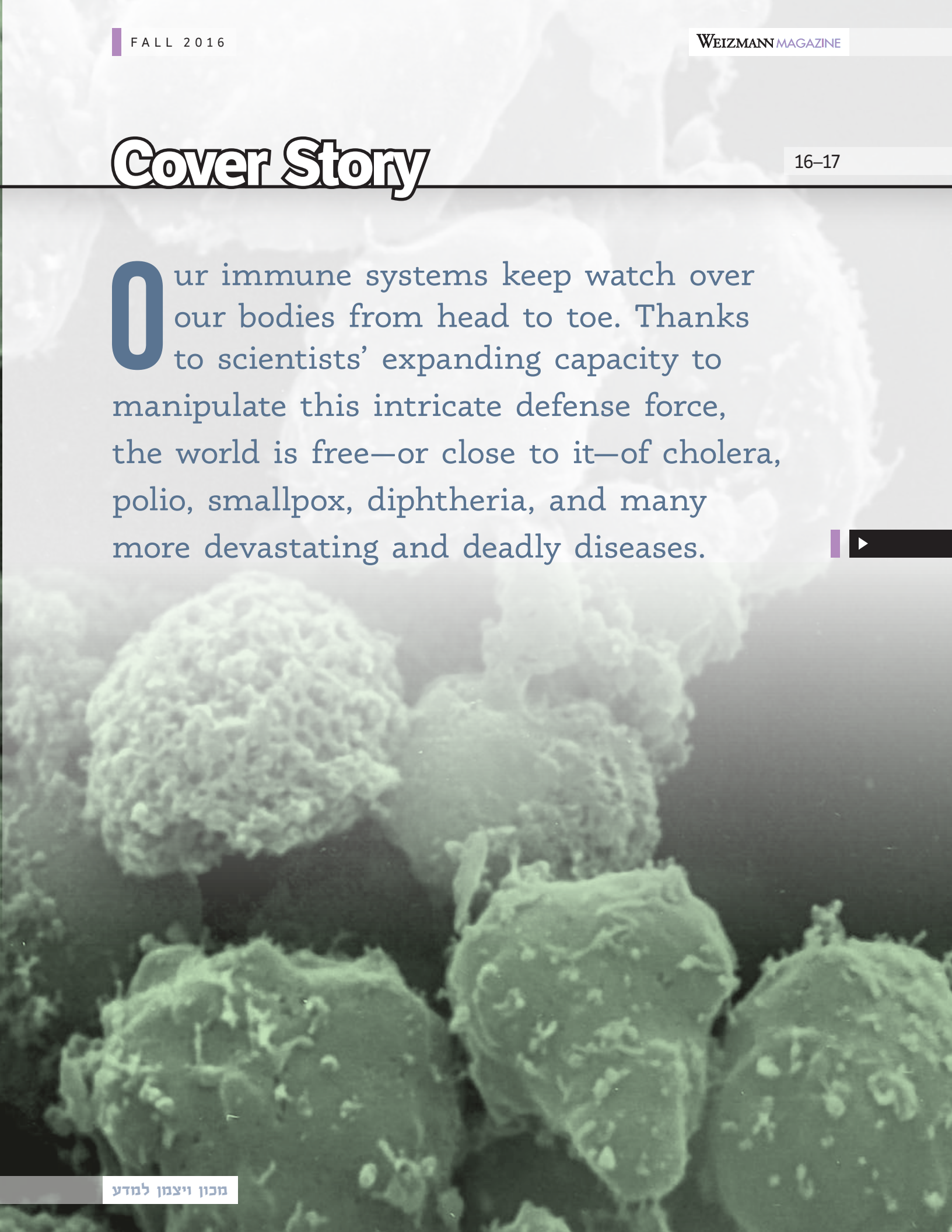
*The immune system is the body's police force, and science is making it stronger*

*Immune system T cells from the lab of Prof. Zelig Eshhar.*

# Cover Story

16–17

Our immune systems keep watch over our bodies from head to toe. Thanks to scientists' expanding capacity to manipulate this intricate defense force, the world is free—or close to it—of cholera, polio, smallpox, diphtheria, and many more devastating and deadly diseases.



Since the first vaccine—for smallpox—was administered over 200 years ago, the study of the immune system, whose complexity rivals that of our brains, continues to yield new, surprising results every day. Unlocking its secrets helps treat autoimmune diseases, in which the immune system mistakenly attacks the body, and recent studies are pointing to ways of manipulating the immune response to treat cancer.

Weizmann Institute research has always been especially strong in immunology, starting with the findings that led to the production of Israel's first ethical drug, Copaxone®, for treating multiple sclerosis, through recent advances in cancer immunotherapy, including a new therapy for leukemia, a method for healing damaged lungs, and more. Among the Weizmann Institute faculty who helped establish the foundations of this field are Institute Prof. Michael Sela (see related story), Prof. Ruth Arnon, Prof. Yair Reisner, and Prof. Zelig Eshhar. All of these veteran scholars and the younger scientists following in their footsteps are proving that an intricate understanding of the immune system can lead to major advances for a wide array of diseases and conditions. The examples abound. Prof. Arnon, for one, went on to elucidate a parasitic disease named bilharzia, devise techniques for targeting cancer cells, and, most recently, she is hard at work developing a universal flu vaccine.

## The rise of cancer immunotherapy

Cancer cells arise from our own cells, but they are also foreign. The immune system does, indeed, know how to identify and destroy many types of cancer cells, but its defenses may be ineffective against cancer growth. Why does the body not mount a proper immune response to cancer? Could the body's natural immune response be heightened and trained to attack cancer cells?

In the 1980s, Prof. Zelig Eshhar of the Department of Immunology was asking these very questions. In his lab at the

*Prof. Zelig Eshhar*

*Cancer cells arise from our own cells, but they are also foreign. The immune system does, indeed, know how to identify and destroy many types of cancer cells, but its defenses may be ineffective against the growth.* 18–19

Weizmann Institute of Science, as well as during a sabbatical year at the U.S. National Institutes of Health, Prof. Eshhar became convinced that the immune system's T cells—highly focused attack forces—could be extracted from the body, modified to identify and eliminate cancer, then reinserted into the body to go to work. While the cancer research community mostly stuck to the conviction that the body's immune response was too weak to combat cancer, Prof. Eshhar was single-minded about pursuing his goal.

Over the next two decades, he worked to make that a reality: He developed a technique for removing immune cells known as "killer T cells" from the subject's blood and genetically engineering them to recognize cells with specific cancer-related proteins on their outer membranes. The process, called "adoptive cell transfer", involves engineering the extracted cells with new receptors known as chimeric antigen receptors, or CARs, that are designed to recognize proteins specifically found on tumors. The modified cells are multiplied outside the body and then re-injected into the patient. These T cells successfully target and destroy the tumor cells in a specific kind of blood cancer called acute lymphoblastic leukemia—and leave the healthy tissue untouched.

Then, in 2013, doctors at several leading medical centers in the U.S. (including the University of Pennsylvania's Abramson Cancer Center, the National Cancer Institute, and MD Anderson) announced that they had adapted Prof. Eshhar's research and used it on patients with terminal leukemia. When three of the first patients treated in Pennsylvania were completely cured, the news rocked the biomedical and pharmaceutical research communities.

Then, in a study at UPenn last year, 27 out of 29 patients with an advanced blood cancer saw their cancers go into remission or disappear altogether following CAR-T cell therapy.

Prof. Eshhar, who recently was awarded the the 2016 Novartis Prize for Clinical Immunology, is now working with the the Santa Monica, California, company Kite Pharma to develop new cancer immunotherapy applications for other cancers, including pancreatic, breast, and prostate cancer that has metastasized to the bone marrow. And he and several members of the research team who trained with him at the Weizmann Institute are conducting research on treating various kinds of cancer at Tel Aviv Sourasky Medical Center, where he heads a research unit. There, treatment of certain hematological cancers will soon start under the supervision of

## From cancer to Alzheimer's

Cancer immunotherapies essentially "turn on" the patient immune system such that exhausted T cells can zero in on the tumor and destroy it. Cancers stop T cells from attacking them, and cancer immunotherapy techniques involve ways to block these inhibitory mechanisms, so that T cells and other immune cells can go back to doing their job and destroying the tumor—as Prof. Zelig Eshhar has successfully done. The current challenge is to understand with greater precision these inhibitory mechanisms—so-called "check-points"—that keep T cells from becoming too numerous and aggressive. In addition, it is still not clearly understood which patients will respond to the existing therapies and which patients will require other types.

Dr. Ido Amit of the Department of Immunology is investigating both of these avenues, which involves identifying the diverse composition of cells and pathways within the tumor ecosystem. To this end, he and his team have developed an experimental and analytical method called "massively parallel single-cell RNA-Sequencing" for measuring the genomic content of hundreds of thousands of cells simultaneously. In investigating one such check point which is relevant in cancer, his team, together with Prof. Michal Schwartz of the Department of Neurobiology, found something surprising: That inhibiting this pathway also prevents the neurodegenerative effects in Alzheimer's disease—opening the way for new approaches to fighting neurodegenerative diseases.

Kite Pharma. In recognition of his work, he received the Israel Prize in 2015 and the prestigious Massry Prize in 2014.

## Healing damaged lungs

Sometimes, a deep understanding of the immune processes that underlie one condition can lead to insight into another, very different one. Prof. Yair Reisner is one of the world's leading experts in preventing immune system rejection of transplanted stem cells. His methods for using bone marrow from mismatched donors have saved the lives of children born with an immune disease called severe combined immune deficiency ("bubble children"), as well as those of many leukemia patients in various European clinical trials.

When bone marrow stem cells are transplanted, patients first undergo radiation to eradicate the stem cells residing within special compartments in the marrow. This enables healthy transplanted cells to repopulate the compartments and begin producing active new blood cells. Prof. Reisner and his group realized that the lung's stem cells, which replace worn out and damaged lung tissue, occupy compartments within the lungs that are very similar to those in the bone marrow. They wondered: In cases of severely damaged lungs, for example in advanced cystic fibrosis, could healthy lung stem cells be transplanted in a similar method to that of bone marrow cells?


*Prof. Yair Reisner*

However, not just any stem cells would do the job. The developmental age of the harvested cells mattered. When the team injected embryonic stem cells from around the 20th week into mice with lung damage, new lung tissue began to appear after about six weeks—and a few months later the lungs were healed. The new challenge is figuring out how such cells might be implanted without requiring massive doses of anti-rejection drugs.

Meanwhile, in turns out that in a type of lung condition called chronic obstructive pulmonary disease (COPD), insights on the immune system are leading to answers as well. Prof. Ronen Alon is studying the interplay between tobacco smoke and different immune cells underlying susceptibility of patients to COPD. His studies shed new light on the activities of a protein, the tumor suppressor DAP-kinase, that triggers the immune system to prompt damaged cells to commit suicide.

He noticed that this critical protein, missing or inactivated in many tumor cell lines, including certain lung cancers, plays an role in suppressing inflammation. His research on other tumor suppressors such as p53 and their role in lung inflammation will help in the identification of risk factors that predispose people to COPD and to specific lung cancers, as well as assist in the elucidation of new links between inflammation, aging, and cancer.

## Building a better antibody

The immune system has an army of antibodies to identify foreign invaders such as viruses and bacteria—and neutralize them. Several recent recruits in the Department of Immunology study how the body's T cell "police" learn how to distinguish friend from foe. The tiny thymus is the source of the body's T cells—immune system cells that patrol the bloodstream looking for foreign invaders.

Theoretically, the body could produce over a billion versions of antibodies. That number "is way more than the body will need in a lifetime," says Dr. Ziv Shulman, who joined the Institute in 2015. "The question is: How does the body choose from all of these possibilities, producing antibodies and tailoring them to specific pathogens, in sufficient quality and quantities?"

Creating antibodies to fight infection involves an intricate dance that takes place in the body's lymph nodes between antibody-producing B cells and T cells. In these interactions, T cells select B cells to produce antibodies in large quantities, and in random

*The immune system has an army of antibodies to identify foreign invaders such as viruses and bacteria—and neutralize them.*



configurations. When an unfamiliar pathogen strikes, a small number of antibodies will grab a piece of the invader and display it, like a war trophy, on the outside of the cell. But sometime between identifying the invader and mounting a all-out attack, B cells become honed to precisely identify and efficiently destroy the pathogen.

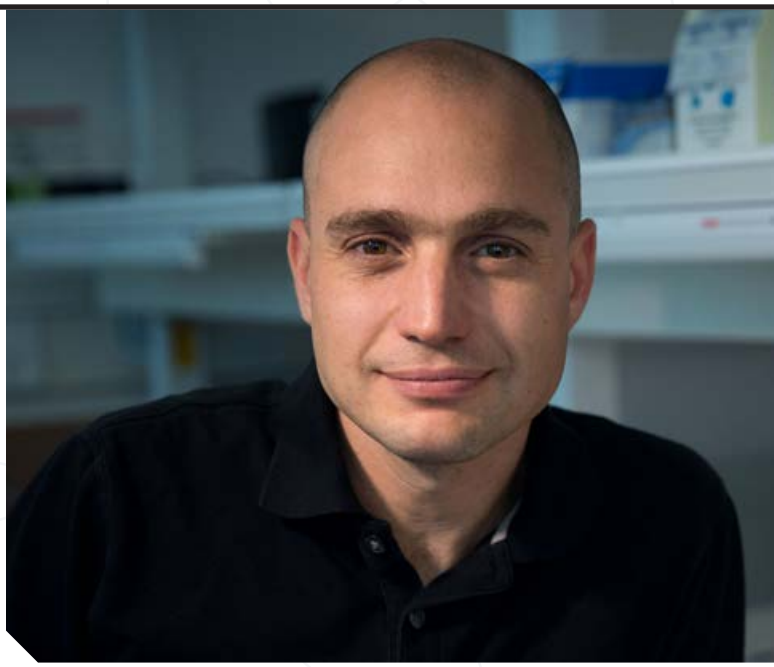
B cells are the only immune cells in the body that purposely mutate their genomes. It takes another type of cell, which Dr. Shulman dubs the "instructor," to select those cells that have mutated their antibody encoding genes in the right direction—towards sporting the most war trophies—and get them to divide and move out of the lymph node "training grounds" and into the bloodstream.

Dr. Shulman focuses on the communication between B cells and their instructors. Understanding this stage of the immune response, he says, may lead to the development of ways to control it. For example, he and his team are investigating the communication between immune cells that keep the gut bacteria contained within the intestines. This could lead to new treatments for such diseases as Crohn's, in which the gut is "leaky," or to oral immunizations for infectious diseases.

They are also creating a method to identify antibodies in cancer patients' B cells. This will allow production and testing of antibodies in the lab and will be adaptable to various treatments, including the antibody component of the CAR-T method developed by Prof. Eshhar.

## Teaching tolerance

A number of the most successful drugs to arise from Weizmann Institute research treat autoimmune diseases—those diseases that occur when the immune system mistakenly attacks the body. These include Rebif®, developed by Prof. Michel Revel, which applies an immune system molecule called interferon beta to treating MS. As well, the work of Prof. David Wallach on inflammatory substances called cytokines led to the development of several



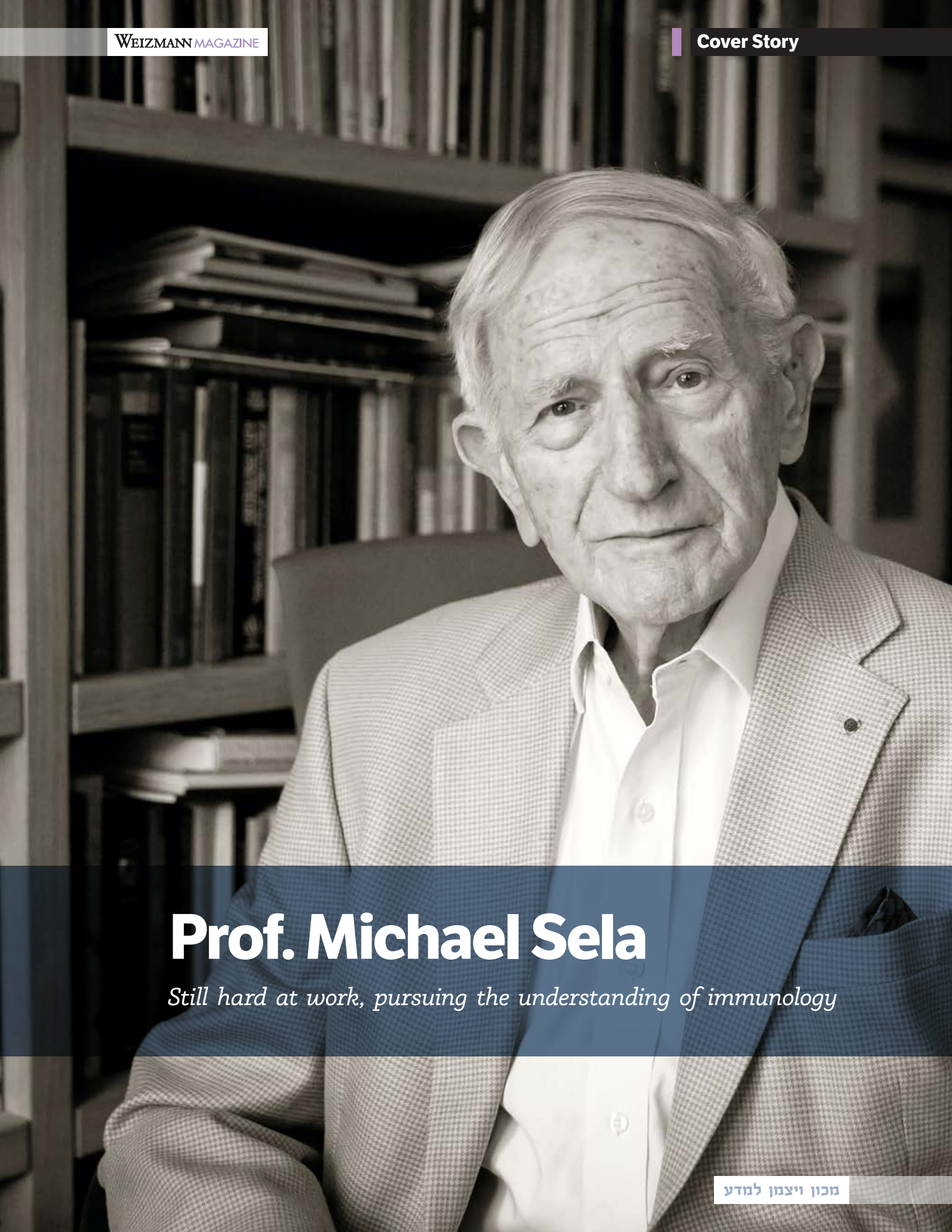
*Dr. Ziv Shulman*

drugs, for such autoimmune diseases as rheumatic arthritis and psoriasis.

New research in this area is extensive. Prof. Idit Shachar, Head of the Department of Immunology, is studying, among other things, the immune system's role in rheumatoid arthritis, an autoimmune disease.

The basic science revolves around the fact that immune system T cells must be "taught" not only how to recognize a foe, but also how to tolerate the body's own components. If T cells don't learn these lessons well, it can lead to damaging autoimmune reactions, which may ultimately result in various diseases, such as type-1 diabetes or multiple sclerosis.

The most critical steps in the process of teaching tolerance to T cells take place in their nursery—the thymus. Strikingly, this process is regulated primarily by a single gene, the autoimmune regulator Aire, which Dr. Kobi Abramson studies extensively. It turns out that Aire is quite a busybody in the thymus, for it not only drives expression of thousands of genes ectopically—in a place where they are not normally found—but most importantly it allows the body to get rid of self-reactive T cells that would otherwise cause autoimmunity.



# Prof. Michael Sela

*Still hard at work, pursuing the understanding of immunology*



The illustrious career of immunologist Prof. Michael Sela has resulted in a widely prescribed drug for multiple sclerosis and several cancer drugs. But he is most proud, he says, of his part in research that did not directly cure disease or result in patents. These were experiments that uncovered the genetic control of the immune response—a finding that would lead to the development of whole new fields of immunology research.

Prof. Sela originally thought he would be a chemist. He arrived in Israel at age 17, after his family had first fled Poland and then Romania. In 1941, shortly after his arrival, he enrolled in the chemistry program at The Hebrew University of Jerusalem. “I was at home with Polish, German, Romanian and French, but not yet with Hebrew and English,” he says. He began learning Hebrew the minute he arrived in Israel; he taught himself English by reading with the aid of a dictionary.

After completing his MSc in Jerusalem, he went to Geneva to conduct PhD studies, but several months later he moved to Italy where he helped whisk European Jews—mostly Holocaust survivors—to Israel. After Israel’s independence was declared, he became a commercial secretary in the Israeli legation in Czechoslovakia. His immediate family had escaped to Israel, but many other relatives had perished at the hands of the Nazis.

But as a young man, he still had his heart set on science. Returning

to Israel in 1950, he joined the newly formed Weizmann Institute of Science and became a student of the renowned biophysicist Prof. Ephraim Katzir. Prof. Katzir worked with poly-amino acids—synthetic models that facilitate the study of proteins. Katzir would later serve as President of the State of Israel, and then return to his lab in the Weizmann Institute.

Prof. Katzir was interested in synthesizing poly-amino acids because they had interesting properties and promised chemical applications, but Prof. Sela—who attained a faculty position at the Weizmann Institute after a postdoc stint at the National Institutes of Health in the U.S.—thought that the same molecules might have biological properties. Specifically, he intuited that such molecules could serve as antigens—molecules that would provoke a unique immune response in the body.


## Serendipity and perseverance

With the goal of better understanding the processes at work in multiple sclerosis (MS), Prof. Sela, Dr. Dvora Teitelbaum, and Prof. Ruth Arnon—Prof. Sela's first PhD student—developed synthetic molecules, and injected them into mice in the hope of inducing the symptoms of MS, an autoimmune disease in which the immune system mistakenly attacks the myelin sheath surrounding the nerve extensions. But the molecules did not work as planned: "We tried to induce the disease using these co-polymers for over a year without success. It later turned out, to our complete surprise, that instead of inducing the disease, the peptides were curing it," he says.

It would take that team another 28 years to get the drug based on this discovery—Copaxone®—to the final stages of FDA approval. Copaxone® was the first drug based on a completely synthetic antigen, and it was Israel's first ethical drug. Along the way, Prof. Sela and others have researched its mode of action, finding that the drug not only slows the destruction of the protective myelin sheath, it can in some cases restore the sheath. Originally licensed to the Israeli pharmaceutical company Teva, Copaxone® is now approved for use in 51 countries.

For Prof. Sela, the findings were proof that synthetic antigens could have significant biological functions. That may seem obvious in hindsight, from our vantage point of designer drugs and computer-designed proteins, but an early paper the group wrote on synthetic antigens was rejected by *Nature*. (It was later published elsewhere and has been named a "Citations Classic.")

Synthetic antigens would enable Prof. Sela, together with John Humphrey of England's National Institute for Medical Research and Hugh McDevitt of Stanford University, to discover the genetic control of the immune response when they observed that the same molecules would produce immune reactions in some strains of lab animals, but not in others. "Of all the contributions of synthetic polypeptides toward our present-day understanding of immunology, none has been more important than the discovery and the definition of the genetic control of the immune response, which in turn, was a crucial trigger toward a better understanding of the cellular basis of immunological responsiveness," he says. Indeed, synthetic polypeptides have since become a mainstay of this area of research.

## Cancer research and beyond

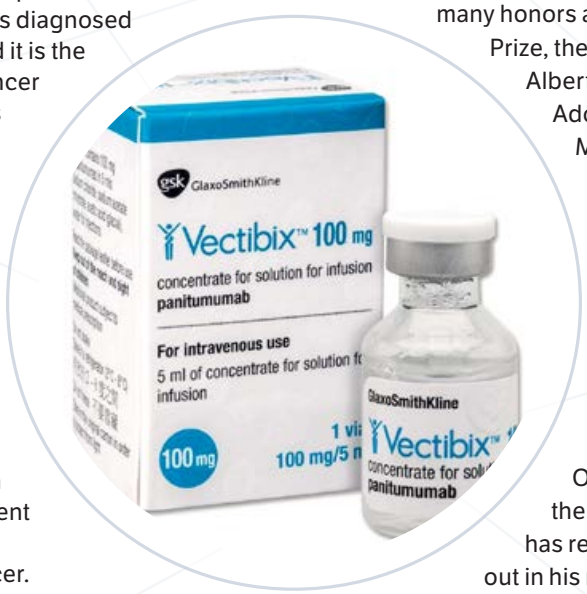
Prof. Sela also turned to cancer research, with the idea of creating small molecules that would block the receptors on cancer cells. This included around

*He has been a source of inspiration for many biologists and biochemists, and refers to his "family tree" of more than 400 students and students of students. "This accomplishment makes me very proud, and also allows me a certain unique perspective," he says.*

24–25

20 years of collaboration with the Prof. Yosef Yarden of the Department of Biological Regulation. Work in his lab group in the 1980s on blocking the cells' growth receptors has led to the development of three anti-cancer drugs to date.

For patients suffering from lung cancer, this year brought good news with the approval by the FDA of a new drug, Portrazza® (Necitumumab). The therapy, administered in combination with two forms of traditional chemotherapy, is used for patients with advanced (metastatic) squamous non-small cell lung cancer. This subtype comprises the major proportion—some 85 percent—of the 220,000 new lung cancer cases diagnosed each year in the U.S. alone, and it is the most common form of lung cancer in non-smokers. Until now, this type of cancer has been very difficult to treat, with few treatment options.




Portrazza® is the third cancer drug to be developed on the basis of a single patent that emerged from Prof. Sela's research. The first one was Erbitux®, manufactured by Merck and Eli Lilly, which was approved in 2009 by the FDA for the treatment of head and neck carcinomas and metastatic colorectal cancer. The second was Vectibix®, manufactured by Amgen, for the treatment of metastatic colorectal cancer.

All three of these drugs are antibodies that block a receptor on the surface of cancer cells, called the epidermal growth factor receptor, EGFR. When certain cancer cells have too much EGFR, they grow faster; thus the receptor plays a role in the formation and spread of cancerous tumors. Used in combination with chemotherapy or radiation, blocking EGFR may prevent cancer from growing. Prof. Sela and two colleagues, Dr. Esther Aboud-Pirak and Dr. Esther Hurwitz, published their observations about EGFR in 1988.

Much of Prof. Sela's later cancer research involved small molecules called aptamers that can be designed to target very specific proteins. He is confident that his research in this field will continue to produce results in the future: "Even if I will not see it in my lifetime, I think that aptamers will become very efficient disease-fighting molecules," he says.

Prof. Sela founded the Weizmann Institute's Chemical Immunology Section (later the Department of Chemical Immunology) in 1963, and served as its head until 1975. He served two terms as Weizmann Institute of Science President, from 1975-1985. His many honors and awards include the Wolf Prize, the Israel Prize, the UNESCO Albert Einstein Gold Medal, and the Adolf von Harnack Medal of the Max-Planck-Gesellshcaft. He is a Commander of the French Legion of Honor, a member of the Pontifical Academy of Sciences, the National Academy of Sciences, and the American Academy of Arts and Sciences; and a founder of the European Molecular Biology Organization (EMBO). Among the numerous awards Prof. Sela has received, the one that stands out in his mind is the Interbrew-Baillet Latour Health Prize, which was conferred on him by the Queen of Belgium.

Prof. Sela set up the Yeda-Sela Fund, which supports basic research projects that may not otherwise win funding from traditional funding agencies. He has been a source of inspiration for many biologists and biochemists, and refers to his "family tree" of more than 400 students and students of students. "This accomplishment makes me very proud, and also allows me a certain unique perspective," he says. To those who would follow in his path, he likes to say: "Pursue your chosen field with great passion, and with a bit of luck, great discoveries will follow."


# The evolving man-machine partnership

*Institute scientists fuse the best of both worlds*

# Science Feature

As much as we love our computers, we humans—not the systems we design—have always maintained the upper hand. At the Weizmann Institute, this "power relationship" is now being re-examined. A number of labs are recalibrating the man-machine connection, by demonstrating how computerized systems can enter into beneficial partnerships with human behaviors related to critical thinking, sight, and even the way we breathe.

As new technologies emerge, the relationship between man and machine grows closer, offering options for injecting automation into a vast range of human activities. At the same time, they open up fascinating questions about how the devices making our lives faster, more accurate, and more powerful, affect society. By pioneering the principles and methodologies that propel the emerging man-machine partnership, Weizmann Institute researchers are contributing design principles for the discoveries yet to come.

*Prof. David Harel*

## Wisdom to work together

"Since the beginning of the computer age, programming has been based on telling a machine exactly what to do, so that the machine can serve us," says Prof. David Harel, a member of the Department of Computer Science and Applied Mathematics. "But we believe that the time has come to shift the balance between man and machine."

Prof. Harel is the creator of breakthrough visual languages for systems design—"Statecharts" in 1984 and "Live Sequence Charts" (LSC) in 1998—which are credited with "liberating" programmers and engineers, by dramatically simplifying the translation of abstract ideas into formal computer code. Now, together with Dr. Assaf Marron and other members of his research team, he has set his sights on launching what he believes will be systems design's next revolution. It's an approach he calls "Wise Computing", in which the computer actually joins the development team as an equal partner—knowledgeable, concerned, and proactively responsible.

Wise Computing involves an intelligent software engineering environment that provides what professional systems developers have come to expect—powerful tools for programming and analysis. In addition, however, it imbues the development suite with knowledge of engineering principles, as well as comprehensive information about the specific, real-world domain in which the system will eventually be used. This gives the computer "experience" to draw on, enabling it to actively contribute to the design process—something that was previously the exclusive purview of human programmers and domain experts.

"Based on this approach," Prof. Harel says, "we enable the computer to participate in an ongoing dialogue. Not only does the computer monitor the human programmer's decisions in real time, it actually takes part in the decision-making process, proactively guiding the programmer towards improved outcomes."

The new approach also mimics and applies powerful capabilities that humans possess, but which are not specific to systems development. "In Wise Computing, the design suite spontaneously notices unexpected patterns in the system's behavior, and categorizes them as desired or undesired," Dr. Marron explains. "It can then propose tests and solutions for detected problems. This unprecedented functionality is possible because at least some of the knowledge, skills, and experience

*Prof. Shimon Ullman*

of human experts has been incorporated into to the design tool itself."

Wise Computing can also reduce errors. "Rather than compose a million lines of code then attempt to carry out after-the-fact verification to check how they work together, Wise Computing will help designers get the overall design right far earlier," Prof. Harel says.

Another advantage of the approach is its sophisticated use of natural language. Together with his former PhD student, Dr. Michal Gordon, Prof. Harel was able, for the first time, to make it possible to use reasonably rich English to write fully executable LSC programs. According to Prof. Harel, this approach represents an important step forward in getting computers to understand the way humans naturally communicate, rather than requiring sets of instructions rendered in formal programming language.

"The computer translates the results of this 'conversation' into code automatically," Prof. Harel says. "Our demo already shows how humans and computers can share responsibility for the creation of a computerized system. But the conversation has really just begun."

## Seeing over the horizon

Computerized vision—think security sensors and the way digital cameras automatically outline faces—is also creeping closer to human capability. Israel Prize winner Prof. Shimon Ullman of the Institute's Department of Computer Science and Applied Mathematics recently identified how the analysis of neural processes governing how the human brain processes visual stimuli may eventually contribute to the creation of more powerful computer vision systems.

The Ullman lab has spawned scientists who have gone on to develop new technologies based on the understanding of sight. For instance, his former student, (Prof.) Amnon Shashua of the Hebrew University, founded Mobileye, the automotive computer-vision startup that went on to become the most successful IPO in Israeli history.

The current story begins with Amazon Mechanical Turk, a research platform used by scientists and technology developers to test their ideas over the Internet, by paying each member of a large cadre of participants a small fee for completing web-based tasks. Prof. Ullman used Mechanical Turk to ask thousands of people to identify a series of images; they were pitted against computers that were programmed to do the same.

Some of these images were successively cut from larger ones, revealing less and less of the original. Others had successive reductions in resolution, with accompanying reductions in detail. Prof. Ullman's team found that humans performed better than computers at identifying partial- or low-resolution images. They also noticed something else: that when the level of detail was reduced to a very specific degree, nearly all the human participants lost their ability to identify the image.

According to Prof. Ullman, this sharp dividing line between recognition and non-recognition indicates a visual recognition hurdle that is structurally hard wired into the human brain. He says that while current computer-based models seek to achieve human-like vision, they do not yet incorporate anything that approximates the human "cut-off point" that he discovered. In short, he says, to truly mimic human sight, there is more work to be done.

"The results of this study indicate that no matter what our life experience or training, object recognition works nearly the same way for everyone," Prof. Ullman says. "The findings also suggest there may be something in our brains that is tuned to optimally process images with a minimal amount of visual information, in a way that current computer models cannot replicate. Such 'atoms of recognition' could prove

valuable tools for brain research, as well as for developing improved computer and robotic vision systems."

And speaking of better computer vision, Prof. Ullman's research also hints at a potential engineering strategy.

"The difference between computer and human visual recognition capabilities may lie in the fact that computer algorithms adopt a 'bottom-up' approach that moves from simple features to complex ones. Human brains, on the other hand, work in 'bottom-up' and 'top-down' modes simultaneously, by comparing the elements in an image to a sort of model stored in memory," Prof. Ullman explains. "Perhaps, by incorporating this bi-directional analysis into automated systems, it may be possible to narrow the performance gap between humans and computers, and make computer-based visual recognition better."

## Sniff and go

*Dr. Anton Plotkin in the lab of Prof. Noam Sobel, testing the sniff-controlled motorized wheelchair.*

In another Weizmann Institute lab, neurobiological studies of another human sense—smell—inspired the creation of a new technology for humans who need mobility assistance: a sniff-controlled motorized wheelchair. This patent-pending invention emerged serendipitously from the laboratory of Prof. Noam Sobel, an expert in the way the brain processes olfactory signals.

"We had been examining sensitivity to particular smells, using an experimental setup in which the sniffing action in participants' noses caused a device to emit an odor," says Prof. Sobel, former head of the Weizmann Institute's Department of Neurobiology. "It suddenly dawned on us that this nasal 'trigger' could be used as a fast and accurate switch for controlling other devices—and that it might be particularly useful for people with physical disabilities."

In 2010, he put his hunch into action, by applying "nose power" to the navigation of motorized wheelchairs. He created a two-sniff code in which two inward sniffs propelled the chair forward, and two outward sniffs reversed it. Different combinations of in-and-out sniffing sent the chair to the right or left. After just 15 minutes of training, a man paralyzed from the neck down successfully drove his wheelchair around an obstacle course—an achievement that made headlines worldwide.

More recently, Prof. Sobel's team reported that human "sniff control" can be combined with computational technologies to solve another problem associated with physical paralysis: the inability of individuals with paralysis to muster the coordinated muscle power needed to produce an effective cough.

"People with high spinal cord injuries typically depend on caregivers to manually assist in coughing by pressing against their abdominal wall," says Dr. Lior Haviv, a staff scientist in Prof. Sobel's lab. "While some technologies exist for stimulating abdominal muscles with surface electrodes, the success of these methods depends on very precise timing. With the use of the sniff controller, our lab significantly improved the ability of people with spinal cord injuries to cough effectively, and without assistance."

Dr. Haviv—who himself uses a wheelchair as the result of a bicycle accident 12 years ago—explains that the "key to the cough" was the exact measurement of nasal airflow. They measured the peak force of the expelled air produced by coughing in subjects with a high spinal cord injury, whose cough was externally stimulated. "While all the assisted techniques we studied improved airflow to a similar degree," he says, "the sniff-control method was the only one that could be activated even by those individuals with severe spinal cord injury. This provides independence that is a critical factor for quality of life."

# Global Gathering




# London 2016

**Top:** *Guests had a unique opportunity to hear the Royal Marine Band play. After asking formal permission from Weizmann Institute President Prof. Daniel Zajfman, the band played "God Save the Queen" and ended with "Hatikva".*
**Bottom:** *New President Circle Members: 17 new members were admitted into the President's Circle in a moving ceremony at the Guildhall in London with some 350 guests in attendance.*

# Special Section



## Learning from the cutting-edge

In five fascinating sessions, seven Institute scientists and Prof. Marcus du Sautoy, Professor for the Public Understanding of Science at Oxford University, presented their cutting-edge research.

Prof. Gabi Barbash, Director of the new Bench-to-Bedside Program, and Prof. Amos Tanay of the Departments of Biological Regulation and Computer Science and Applied Mathematics, spoke about personalized medicine and their program's plans to integrate anonymized patient data into scientific research.

Prof. Michal Irani of the Department of Computer Science and Applied Mathematics and Prof. Lucio Frydman of the Department of Chemical Physics both spoke about "Seeing the Invisible". Prof. Irani spoke about computer algorithms that can complete visual scenes, and Prof. Frydman discussed the past, present, and future of magnetic resonance research.

Prof. Marcus du Sautoy, and Prof. Roee Ozeri of the Department of Physics of Complex Systems, spoke about the "things we can and cannot know": whether there is a limit to scientific knowledge. One thing we can know, claimed Prof. Ozeri, is there is vast potential of quantum mechanics for the future of computing.

Up next was a session featuring new scientists at the Institute. Dr. Ruth Scherz-Shouval of the Department of Biomolecular Sciences described the so-called "microenvironments" surrounding tumors and Dr. Ziv Shulman of the Department of Immunology described how the body selects the best antibodies to fight disease, including cancer.

The scientific session concluded with a "Crystal Ball" discussion in which the scientists speculated about future scientific developments and their impact on mankind.


*L to R: Profs. Lucio Frydman, Michal Irani, and Roee Ozeri*

# Q&A with Prof. Marcus du Sautoy

Curiosity may have no boundaries, but will we ever reach a point at which we know everything? This is a burning question for Prof. Marcus du Sautoy, who explored the answers in his guest talk at the Global Gathering. It is also the topic of his latest book, *What We Cannot Know: Explorations at the Edge of Knowledge* (2016).

Prof. du Sautoy is a Professor of Mathematics at the University of Oxford and the Simonyi Professor for the Public Understanding of Science, and is a frequent contributor to the BBC and other UK media. In 2009 the Royal Society awarded him the Faraday Prize for excellence in communicating science to the public, and in 2010 he received an OBE from the Queen for his services to science. He is a fellow of the Royal Society. *Weizmann Magazine* had some questions of its own for the expert science communicator.

**Q Why do the unknowns intrigue you?**

**A** The sense of not knowing what's ahead is what makes life worth living. This is true in science, and in our own lives. It is the unsolved problems that drive science that make it a living, breathing subject. It was the conjectures that I couldn't solve as a mathematician that first drove me to visit Israel in the search for solutions. I did my postdoctoral research at The Hebrew University of Jerusalem, where I met Alex Lubotzky [former chairman of the Einstein Institute of Mathematics] in 1992. Alex has very different political views than I do; he lives in Efrat on the West Bank; and he's an Orthodox Jew. I was a left-wing atheist whose only religion was football. But we realized that we spoke the same language. We were able to connect immediately; it was like meeting a long-lost brother. That's the beautiful thing about maths and science—it's a language that brings people together.

I fell in love with Israel, traveled everywhere, and gave lectures in many places, including at the Weizmann Institute. And I met my wife, Shani, who was studying

at Bezalel. I came back to the UK with a theorem and a wife.

In science, we have turned over so many stones, illuminating so many unexpected things. But that has made me think: Is there a limit to what we can know? I am a product of the Oxford system, where you spend a lot of time with people outside your discipline, to be broad-minded. This is how I learned about the theologian Herbert McCabe, who declared that 'to assert the existence of God is to claim that there is an unanswered question about the universe.' And this brought me to the question at the heart of my new book: 'Can we identify things that will always remain beyond knowledge?'

**Q Mathematicians don't typically spend their time communicating science to the masses. Why do you do it?**

**A** My initial career trajectory was a pure scientific one, but the climate in science has changed. There is an awareness that science is having a massive

impact on society and we are going to need to understand science in order to make major decisions about directions in which society should go. Take stem cells: If you don't understand what a stem cell is, you are disenfranchised from any debate about their use. So, especially in the UK, there is a realization that it is the responsibility for scientists not just to make the big discoveries but also to communicate to the public what they've discovered.

In 1995 I received a 10-year research fellowship from the Royal Society to continue the research I had started as a postdoc in Israel. Since I didn't have any teaching duties it gave me the space also to explore communicating some of the breakthroughs that were happening in my area of mathematics to a wider audience. I have always believed that science is about discovery and communication—that it is the responsibility of scientists to explain science. What is a discovery if it isn't communicated? Knowledge doesn't exist if it's just in your own head. It has to exist in other people's heads. The Royal Society was very supportive of these efforts to communicate science to the public especially because there was a recognition that science was having an ever bigger impact on society.

The communication work I did culminated in 2008 in my appointment to the Simonyi professorship, which had been established by Charles Simonyi [who built Microsoft's profitable products Microsoft Word and Excel]. Oxford was very farsighted by creating a named professorship that carves out time and funds for scientists to communicate science to the public. I make TV and radio programs, write books, speak everywhere I can, and I have trained a small army of Oxford students to go out to schools and talk about the value of science and maths.

We are trying to fight the ease with which people say they are bad at math and wear it as a badge of honor. The prevailing approach in education has been that there is science and there is humanities—never the twain shall meet. I'm working to make sure people see the two as fully integrated.

***"What is a discovery if it isn't communicated?"***

**Q What does the public need to understand most?**

**A** The impact of machine learning on society. Are you going to trust an algorithm to manage your health? It's ultimately going to be better than your doctor, but people's first reaction will probably be negative. So people need to understand what algorithms are and why they matter.

Even between scientists, communication must improve. It's hard for a biologist to talk to a mathematician, a physicist to a chemist: It is as if they are from foreign countries. There are many areas in which there is cross-over, and that's where all the exciting stuff is happening. I know this is happening at Weizmann. But science remains like a foreign country for many people. So I see my role as an ambassador for the 'superpower of science'.

**Q Why do you love math and science?**

**A** Scientists are driven by the basic desire to know. It is a basic human trait. Just by understanding, we can change the universe, for good. The Weizmann knows this, and does it extremely well; that is why, when I learned about the Weizmann Institute's *Science on Tap* [science talks at pubs] I got involved in a similar series here in the UK. We call it *A Pint of Science*. And the Global Gathering is also a great platform to tell many good stories about science.

For me one of the most exciting things about being a scientist is being part of a good story that goes back to Galileo and Newton. Each new generation is taking the baton and running with it. It is a wonderful time to be a scientist. It feels like a new Newtonian age.

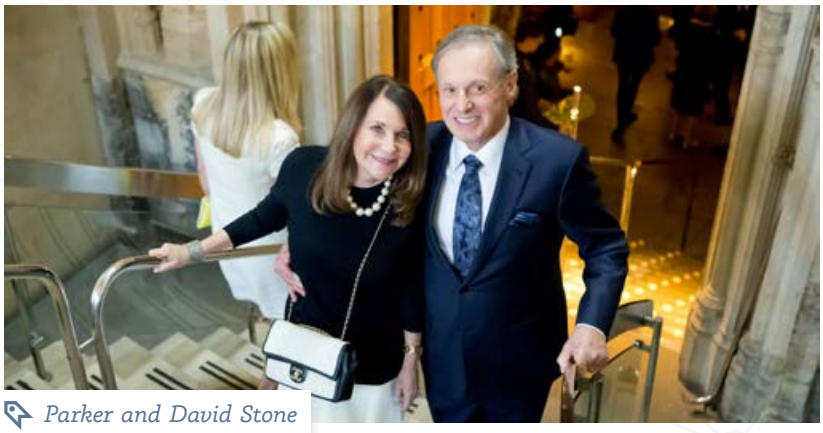
Prof. du Sautoy is the also the author of *The Music of the Primes: Why an Unsolved Problem in Mathematics Matters; Finding Moonshine: A Mathematician's Journey Through Symmetry; and The Number Mysteries: A Mathematical Odyssey through Everyday Life.*

Dr. Manfred Gentz Ingrid Gentz and Christian Tidona Germany

Bob Drake, Ellen Shapiro, Renee Drake

Luis and Lilian Stuhlberger


Weizmann UK Chairman Martin Paisner CBE



Parker and David Stone


Yael and Rami Ungar

Modi Segal and Francie Klein


Barry Townsley CBE, President of Weizmann UK

David Lopatie, Arlyn Imberman, and Pauline and Daniel Auerbach

Simone Licht, Charles Rothschild, Roberto Moritz, and Claudia Rothschild

Dr. Uri Arnon, Sir Paul Nurse, and Prof. Ruth Arnon

Laura Gudelsky, Shelley Mullitz, and Arlene Kaufman

Ellen Merlo; Judy and David Dangoor

Dame Vivian Duffield and Prof. Daniel Zajfman


# Q&A with Dr. Merry Rubin Sherman

When Merry Sherman was a PhD student at the University of California at Berkeley in the 1960s, she attended a course by Prof. Aharon Katzir, a visiting professor from the Weizmann Institute. In 2016, some 50 years later, she has established a professorial chair to memorialize the renowned scientist and his younger brother, Prof. Ephraim Katzir, a biophysicist and Israel's fourth President. Dr. Sherman talked with *Weizmann Magazine* at the Global Gathering about her long relationship with the Katzir family and a lifetime devoted to science. She is currently the CEO of Mountain View Pharmaceuticals, Inc., in Menlo Park, California.

**Q How did you get to know the Katzir brothers?**

**A** I was mesmerized by Aharon's course at Berkeley. His lectures were enchanting, even though his conclusion was sometimes just an equation. The course was on non-equilibrium thermodynamics—the physics of life itself—and he was writing a book on that subject, which he invited me to help him edit. Later, he became a co-author on the publication of some of my thesis research. It was on a topic in which he wasn't involved, but he helped me approach the subject in an original and insightful way.

I was sufficiently inspired by him that when I finished my PhD in the summer of 1966, I came to the Weizmann Institute for my postdoctoral training in Aharon's lab, where I worked on polymers [molecules comprised of repeated subunits, which have been critical for the later development of several long-acting biologic drugs]. During my year at Weizmann, I got to know Ephraim Katzir, whose oldest child had tragically died a few months earlier. Ephraim and his wife, Nina, invited me to live with their family and to be a surrogate big sister to their two younger children. So I had the extraordinary privilege of having Aharon Katzir as my mentor and living with Ephraim Katzir's family. At all hours of the day and night, brilliant scientists and students stopped by the house. It was a hub of intellectual activity.

**Q Why did you stay in Israel during the Six Day War?**

**A** My postdoc was nearly finished and the war was clearly imminent, but I felt committed to stay and was able to help Ephraim in his role as Chief Scientist of the Israel Defense Ministry. A few months later, I returned to the States for a second postdoctoral fellowship at the U.S. National Institutes of Health (NIH), but continued to collaborate with Aharon and published two more scientific reports with him. Then, on May 29, 1972, while I was working at Memorial Sloan-Kettering Cancer Center in New York, I heard that there had been a terrorist incident at Lod Airport [now Ben Gurion Airport] and that a famous Israeli scientist was among the victims. I dreaded immediately that it was either Aharon or Ephraim. A phone call to Israel confirmed that Aharon had been killed, along with 25 others, by members of the Japanese Red Army, trained by Palestinian terrorists. I flew back to Israel for Aharon's funeral with his daughter, Yael, who was studying at Berkeley, and Ephraim met us on the tarmac. I stayed at Ephraim's home during the *shiva*, and everyone — generals, scientists, politicians — came by to share their memories of Aharon's and Ephraim's roles in the early years of Israel and of the Weizmann Institute. I remember that week as vividly as if it were last week.

*Dr. Merry Sherman with the late Prof. Ephraim Katzir*

**Q How did your research result in a drug for gout?**

**A** Although I didn't return to Israel for the first 10 years after Aharon's murder, I kept in touch with Ephraim and visited him often during the next three decades, until his death in 2009. My husband, Dr. Mark Saifer, and I and our colleagues developed a drug for gout, which is caused by the buildup of crystals of uric acid in the joints and tissues. In 1996, when I came to Israel to celebrate Ephraim's 80th birthday, he introduced me to the company that, 20 years later, still produces the drug, Krystexxa®—Bio-Technology General (Israel) Ltd. Our drug is being manufactured in Israel because of Ephraim, and it was developed, in part, based on the knowledge that I gained so many years earlier working with Aharon. It consists of a novel polymer-coupled enzyme called uricase.

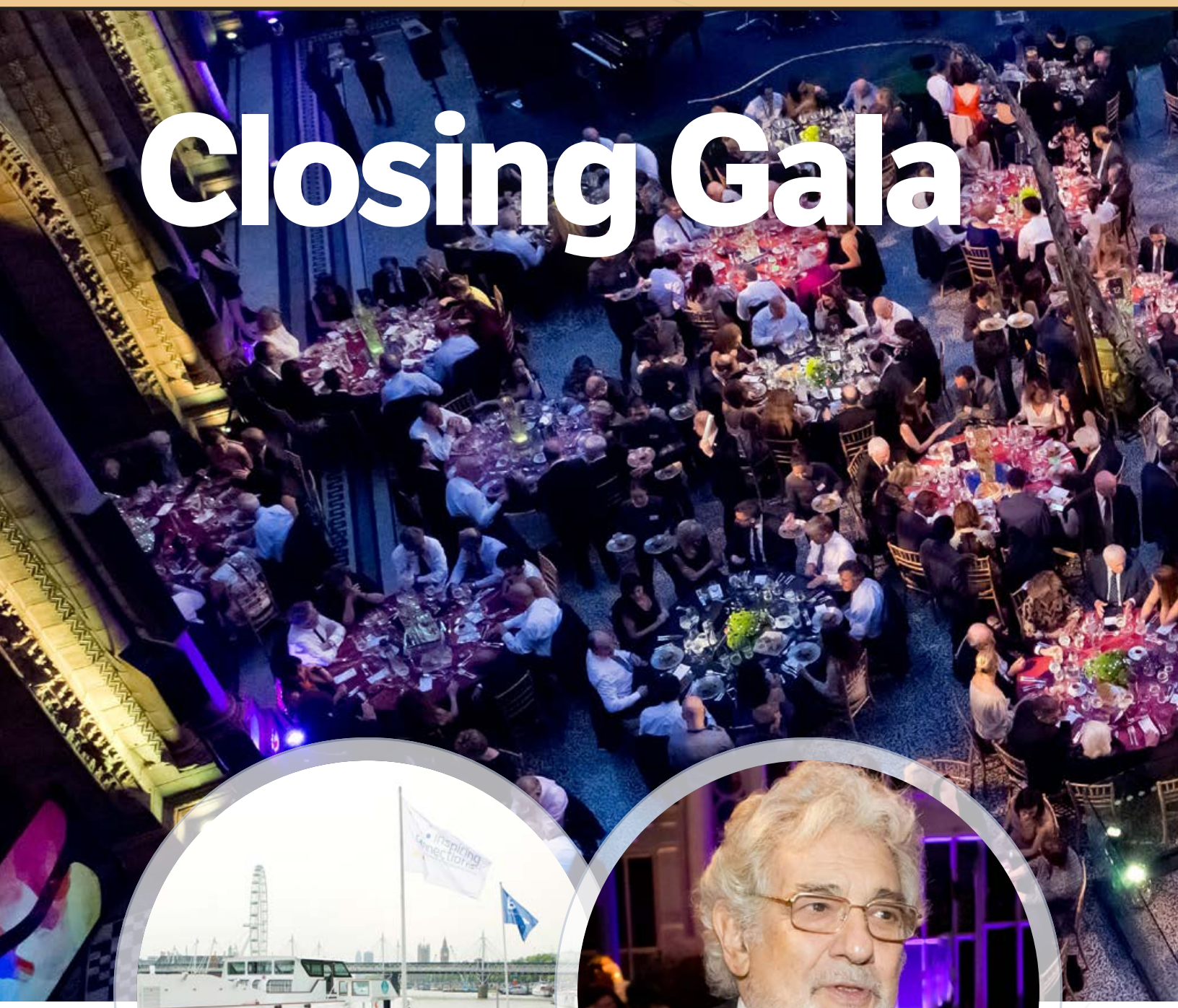
In the U.S., about eight million people suffer from gout, of whom about three million are treated for it. Our drug is intended for use by about 50,000 people, who have the most severe form of the disease. It is an orphan drug with a niche market, but has life-altering effects on patients with the very worst disabilities. They comprise a few percent of treated gout patients who are unresponsive or allergic to allopurinol or the other oral drugs to which most gout patients respond. (The U.S. FDA approved Krystexxa® in 2010 and the European Medicines Agency approved it in 2013.)

**Q Why did you establish a professorial chair?**

**A** It is my way of thanking and honoring the Institute and two of its founding scientists. The Aharon and Ephraim Katzir Memorial Professorial Chair seemed like the best way for me to help preserve the memory of these great Israeli patriots and brilliant scientists. I am delighted that the first incumbent will be a woman (Prof. Michal Sharon of the Department of Biomolecular Sciences), and that her field of research would have intrigued Aharon and Ephraim. I look forward to hearing about the progress of her research in the years ahead, and to forging a friendship with her.

*Following her fellowship at NIH, Dr. Sherman directed research in endocrine biochemistry at Memorial Sloan-Kettering Cancer Center. She later served as a Professor of Biochemistry at Rutgers University in New Jersey before co-founding Mountain View Pharmaceuticals, Inc., in 1995. She is a co-inventor on 11 U.S. patents and more than 270 foreign patents. She has been an Institute supporter for more than 40 years, and serves on the Northern California Regional Board and the National Board of Directors of the American Committee. She was inducted into the President's Circle at the Global Gathering on June 5.*

# Closing Gala








Global Gathering guests were treated to a night at the Royal Opera House for a debut of Verdi's Nabucco starring virtuoso Plácido Domingo, followed by light cocktails. The Silver Sturgeon took guests on an afternoon lunch cruise on the Thames River.



The Closing Gala began at the Victoria and Albert Museum for cocktails, and a duo of bagpipers escorted the guests to the Natural History Museum. The event highlighted the contribution of UK donors to the Weizmann Institute, focusing on funds raised for the the renovation and construction of the Weizmann UK Building for Biocomplexity Research. The nearly 500 guests in attendance were treated to an original song by entertainer Joe Stilgoe about the Weizmann Institute and an address by HE Mark Regev, Israel's ambassador to the UK.


# Where discussion drives discovery

*The Schwartz/Reisman Institute for Theoretical Physics*

# Science Feature

40–41

The massive laboratories where scientists probe the nature of the universe – think the Large Hadron Collider near Geneva, or the Synchrotron Radiation Laboratory in Shanghai – can cost millions or even billions of dollars to build. But in the world of theoretical physics, the smartest possible investment simply involves gathering the best minds together where the conversation—like the coffee—can freely flow.

This is the "business model" behind an exciting new initiative at the Weizmann Institute of Science: the Schwartz/Reisman Institute for Theoretical Physics.

"Discussion drives discovery," says Prof. Eli Waxman, a theoretical astrophysicist who serves as director of the new Institute. "Unlike professional conferences, which are often rigidly structured, we hope to create an open environment that will encourage the emergence of new ideas."

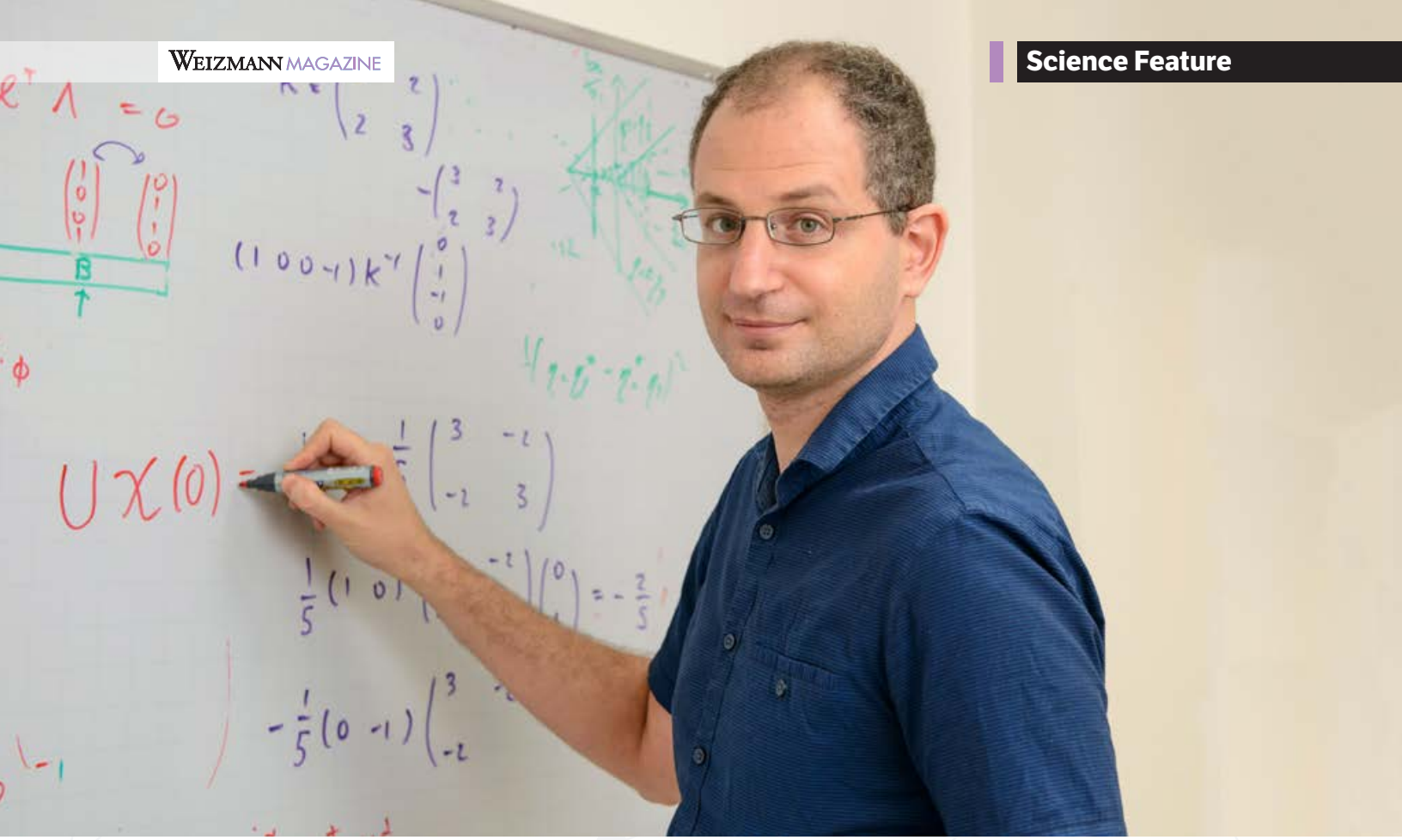

*The Nella and Leon Benoziyo Physics Library, location of the SRITP workshops.*

Established by a major gift from Gerald Schwartz and Heather Reisman of Toronto, the Institute of Theoretical Physics, or ITP, has a three-fold mission: to highlight the exceptional theoretical physics work being done at the Institute, to attract world-leading theoreticians to the campus, and to create the personal connections that can lead to fruitful international collaboration.

Mr. Schwartz and Ms. Reisman have also funded the Schwartz/Reisman Center for Science Education in Rehovot and a series of other educational centers to be established in other locations in Israel; and the research of Prof. Victor Malka of the Institute's Department of Physics of Complex Systems.

Following the successful model established by a handful of other theoretical physics institutions—most notably at the University of California-Santa Barbara, and also including Germany's Johannes Gutenberg University of Mainz—ITP "conversations" are kicked off in the context of specialized, on-campus workshops. Scheduled approximately four times per year and lasting up to two weeks each, these workshops attract a diverse cadre of senior researchers, postdocs and students from around the globe.

Participants in the inaugural workshop at the Weizmann Institute, which took place in the spring, included theoreticians from Harvard, MIT, Cambridge, CERN, the Tata Institute of Fundamental Research in Mumbai, and many other leading



*Dr. Erez Berg will host the second workshop, on subject of quantum states of matter.*

institutions, with local stars from Israeli academia. Entitled "Cosmological Probes of Fundamental Physics," the workshop was conceived of and hosted by Dr. Kfir Blum who says that, due to dramatic changes in the way we observe and measure cosmological phenomena, it's time for a dramatic change in the conversation.

"Scientists are swimming in new data, thanks to state-of-the-art detection techniques," he says. "With three lectures a day plus plenty of free time for informal discussion, we examined how these revolutionary developments are affecting the way we approach the big questions. It was a very rewarding event."

The second workshop, scheduled for December, will be hosted by Dr. Erez Berg of the Department of Condensed Matter Physics. The subject: quantum phases of matter. "The subject is rich in terms of theory, but also has plenty of practical significance—for instance, establishing the principles needed to design new materials," Dr. Berg says, adding that the workshop will also focus on the unexpected convergence between condensed matter physics, high energy physics, and quantum information theory. "For most of the participants, this will be their first visit, and I'm looking forward to introducing them to Israel, as well as to the great work being done here."

In physics, theory can lead to new experimental approaches, something that ITP director Prof. Waxman knows from personal experience.

He models transient emissions from deep space, something scientists know about theoretically, but which is difficult to measure. He is working on a practical Israeli-American project that aims to develop a mini-satellite for detecting the emissions that he and his team have predicted (see opposite page). "If the satellite project is successful," he says, "it will allow us to study stellar explosions and the dynamics associated with super-massive black holes. It may also help detect the source of gravitational waves—ripples in the fabric of space-time predicted by Einstein back in 1915, but first observed by astronomers just this year. As a theoretician, I never planned to go into the satellite-building business. But you never know where the theory will take you."

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# What else is up in physics: a new mini-satellite

Extra-terrestrial observatories like the Hubble Space Telescope—launched a quarter-century ago—have produced images of deep space that helped scientists determine the age of the universe. Now, a Weizmann Institute scientist is enabling the launch of a new type of space satellite capable of capturing near-real time "snaps" of transient explosive events, such as the supernovae flares that mark the death of massive stars.

ULTRASAT is a mini-satellite being developed jointly by Israel and the U.S. Prof. Eli Waxman, of the Department of Particle Physics and Astrophysics, is directing this project, along with colleagues at NASA and the California Institute of Technology. Scheduled for launch in 2021, the new satellite will be capable of measuring the early ultraviolet (UV) emission from transient explosions minutes after they occur—not the days or weeks required using existing technology.

"Most large, space-based telescopes have small fields of view because they track very specific targets," Prof. Waxman says. "ULTRASAT, on the other hand, is designed to observe and record cosmic events that we don't know about in advance, via a field of view 300 times wider than the most powerful UV satellite ever launched. This relatively small satellite will alert the larger ground- and space-based observatories almost immediately, allowing scientists to follow events as they unfold."

If successful, the new satellite—which costs "just" $100 million including launch—will demonstrate how significant scientific value can be achieved with a relatively small monetary investment. ULTRASAT's small size and mass—less than a cubic meter in volume and, at 150 kg, weighing far less than typical satellites launched under the NASA Medium and Small Explorer program—enable this savings.

ULTRASAT will also mark a major step forward for the Israeli aerospace industry. "Israel leads in small defense satellites, but ULTRASAT will put Israel 'on the map' for satellites devoted to research," Prof. Waxman says. "Like SpaceIL, the national initiative to land the first Israeli spacecraft on the moon, ULTRASAT will inspire Israel's young people to study science and technology."

In addition to "on-the-spot-reporting" of emerging supernovae, ULTRASAT will provide data about additional cosmic events characterized by transient explosions.

"We are interested in examining how stars are disrupted—swallowed up—by super-massive black holes," Prof. Waxman says. "We predict that our satellite will identify anywhere from dozens to hundreds of such events each year." It will also help scientists gather evidence about the nature of gravitational waves, a phenomenon first hypothesized 100 years ago in Einstein's general theory of relativity.

*The explosion that resulted in this formation of ionized gas from a long-dead star was an example of an especially energetic and bright variety of supernovae.*

# Rina Mayer

*A family affair, and a slice of Weizmann history*

Few family histories are as deeply intertwined with the history of the Weizmann Institute of Science as that of the family of Rina Mayer—and at the same time, the history of the early development of the State of Israel itself.

Rina's parents, the late Sara and Moshe Mayer, were among the country's financial elite, and Rina spent her childhood moving between Tel Aviv, London, and Switzerland as a consequence of her father's real estate enterprises. It was those enterprises that brought him together with Sir Isaac Wolfson and Sir Charles Clore of the UK, who made some of their first investments in Israel with Mayer—and they in turn brought Sara and Moshe Mayer into their small circle of friends who were early supporters and shapers of the Weizmann Institute. The guests around her parents' dinner table included other central figures at the Institute, including Meir Weisgal and his wife. (Weisgal was Dr. Chaim Weizmann's personal assistant and served in various leadership roles).

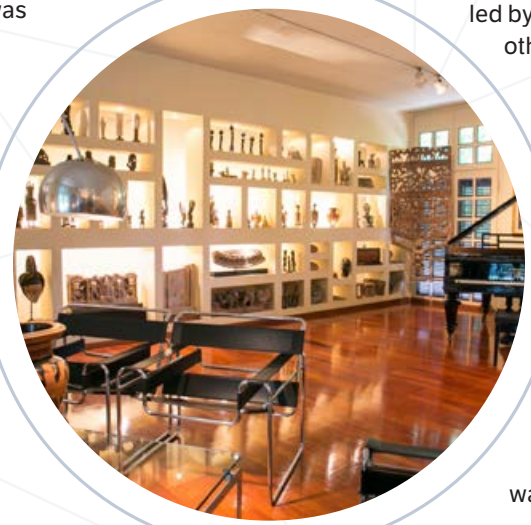
Sir Isaac Wolfson, one of the "founding fathers" of the Institute thanks to his philanthropy and business acumen, first met the Mayer brothers in 1955 and purchased a quarter of the stock of their Export Bank; it was among Sir Isaac's first investments in Israel. His friend Sir Charles Clore later followed suit. Then, in 1961, the Mayer brothers, together with Sir Isaac and Sir Charles and the Israeli government, opened an investment company together,

# Spotlight On



Wolfson Clore Mayer Corp. Ltd., which has made numerous investments in Israel throughout the years, primarily in real estate and construction. The partnership lasted until 1976, when Sir Isaac sold his share to the Mayer brothers. Rina serves as its chairperson today.

Rina lives in Savyon, where she was one of the town's early residents and where she raised her two boys, Danny and Jonathan, and her daughter Andrea. Jonathan and Rina are Institute board members.



*Rina Mayer's home in Savyon, which houses her African and world art collection*

## Out of Africa

When the Israeli daily *Ha'aretz* published an in-depth story about Moshe Mayer's business interests in Africa and Israel in 1970, when Mayer was 61, it declared, "The State of Israel is too small for Moshe Mayer. He is constructing housing, skyscrapers, and luxury hotels, and building rivieras and presidential palaces."

Mayer was a self-made man who developed real estate projects in pre-state Israel and managed some 50 development companies worldwide, from resorts in the Catskills to the Shalom Meir Tower in Tel Aviv, named for his father. At the time it was built, in 1965, it was the tallest skyscraper in the Middle East, though it caused controversy because the historic Herzliya Hebrew Gymnasium was razed for its construction.

In the 1960s, he was one of the first Israelis to eye West Africa for its investment potential. In 1970, he completed the construction of Hotel Ivoire in the Ivory Coast, which was hailed at the time as the most beautiful hotel in the world, and then went on to develop an entire tropical city around it, known as the African Riviera. The African Riviera was planned by a team of Israeli architects—headed by Rina's husband at the time, Thomas Leitersdorf—and funded by international financial bodies.

That development work wasn't simply money in the pocket of Moshe Mayer and his two brothers, who worked with him. It paved the way for an unprecedented process of modernization led by Israelis in the Ivory Coast and other West African countries. Israel began exporting technologies and agricultural expertise and established new infrastructure. Israeli architects and planners even aided in drawing up national master plans for Chad and Sierra Leone; communal settlements reminiscent of the kibbutz were established; and public housing similar to that erected in Israel in the 1950s was constructed.

This tight relationship with Africa lasted until the late 1970s, when the Six Day War and the Yom Kippur War turned the tide of political opinion in Africa vis-à-vis Israel. Leitersdorf went on to a successful career in architecture in Israel, including planning the sprawling Jerusalem suburb of Ma'aleh Adumim. Mayer turned his attentions elsewhere, having laid the seeds for his businesses in Israel, Europe, and the U.S. long before.

## Backstory in Baku

That nucleus of philanthropic families, however, was not the Mayer family's first brush with the Institute. Sara Mayer was born into the Itskovich family (on her mother's side), which owned lucrative oil and gas businesses in Baku, Azerbaijan, before coming to Palestine. In Baku, Sara's maternal grandparents had connections to the Nobel family—for which the Nobel Prizes were named—which ran the most

*Sculptures in Rina Mayer's garden, created by her late son Danny*

lucrative oil company in Baku, on the shores of the Caspian Sea.

The Itskoviches were prominent members of the Jewish community and were well-known in Zionist circles abroad, corresponding at times with Dr. Chaim Weizmann before his establishment of the Daniel Sieff Institute in 1934, which later became the Weizmann Institute of Science. In fact, Rina's maternal grandparents were among the prime movers of many fundraising campaigns to promote the colonization of Palestine. In 1912, the family made a major contribution for the construction of the Hebrew University of Jerusalem.

## A deep Weizmann connection

The relationship between the Mayer family and the Weizmann Institute unfolded over the course of several decades. Among their gifts was the establishment of the Sara and Moshe Mayer Lab for Prof. Robert Fluhr of the Department of Plant and Environmental Sciences.

Sara received an honorary doctorate from the Institute in 1997. Upon her death in 2002, Prof. Ilan Chet, then-President of the Weizmann Institute, wrote in a condolence letter to Rina, "Your mother was among the most generous, caring, and committed Israeli friends of the Institute... She and your late father helped develop and advance the Institute throughout 30 years." The Institute created the Sara Mayer Playground in her memory in 2003.

## Art, fashion, politics: another slice of family history

The Mayer family was intricately connected to many aspects of Israel's history in the arts, culture and politics.

Rina's sister Kena is married to the politician Zalman Shoval, who served as ambassador to the U.S. and was a member of Knesset. Her mother-in-law was the late Finy Leitersdorf, who was known as the mother of Israeli fashion and lived with her son and daughter-in-law in her later years. Finy was the widow of artist Yohanan Simon, known for his murals and paintings which appeared in public buildings and hotels throughout Israel. Rina maintains a collection of Simon's works and Finy's fashion collection in her house in Savyon.

*"I feel a special closeness to the origins of the Institute through my mother's family, and of course the many decades throughout which my parents were involved," says Rina.*



"I feel a special closeness to the origins of the Institute through my mother's family, and of course the many decades throughout which my parents were involved," says Rina. "And my connection only strengthened as I became involved on my own."

During her service in the intelligence unit of the Israel Defense Forces, she came to the Institute once a week to do decoding work on WEIZAC, the first computer in the Middle East, housed in the Ziskind Building.

Years later, following his full term of military service, her son Danny was diagnosed with schizophrenia and Rina became driven to better understand the biological origins of the disease.

In 1994, Rina's family invested in Neurogenic (via Yeda, the Institute's tech transfer arm), a company established as the result of research conducted by Prof. Meir Shinitzky, a member of the Department of Biological Chemistry, for the purpose of developing a blood test for the diagnosis of schizophrenia. Rina has religiously followed the ongoing work of Institute scientists throughout the years and continues to be engaged today. She has given generously to the Institute, including to the Davidson Institute of Science Education and its School of Contemporary Science, and to support new scientists, as well as general research.

*L to R: Mordechai Mayer, Sir Isaac Wolfson, Benjamin Mayer, Sr Charles Clore, Moshe Mayer*

# Israeli Science Club event: love and money

The recent Science Club event of the Israel Friends Association of the Weizmann Institute of Science hosted Dr. Liat Yakir, who talked about the science of love. Dr. Yakir, a graduate of the Department of Molecular Genetics, described a phenomenon in our brains related to falling in love, its effect on choosing whom to fall in love with, and on choosing partners. She asked members of the audience to give compliments or to use affectionate phrases to the people sitting next to them, and measure their response. Her point: to demonstrate the importance of the hormone oxytocin, also known as the "love hormone," which influences making social connections.

Amir Levi, Director of the Budgets Department at Israel's Ministry of Finance, gave a behind-the-scenes look at government economic activity and talked about the effects of Israel's political and security changes on the economy.

# Europe launches young leadership club

About 120 people were in attendance for the launch of the European Committee's new young leadership club, the Weizmann Young European Network (WYEN), in Berlin on June 23. The main guest speaker was **Uri Levine**, founder of Waze, the driving and navigation app that was acquired by Google in 2013. Mr. Levine, who has also founded several other companies, described how he chooses his business ventures and why science and technology matter in the quest to improve lives. WYEN is chaired by **Dr. Christian Tidona** of Heidelberg. Prof. Daniel Zajfman, Weizmann Institute President, spoke, as did Prof. Oded Aharonson of the Department of Earth and Planetary Sciences, and Prof. Yardena Samuels of the Department of Molecular Cell Biology, who spoke about genetics and cancer. Prof. Avishay Gal-Yam of the Department of Particle Physics and Astrophysics talked about colliding and exploding stars.

# Weizmann World



*L to R: Jose Harari (a grandson), Sarah Uziel, and Rolando Uziel*

## New Uziel lab, chair

Sarah and Rolando Uziel of Mexico were on campus on July 14 for a dedication ceremony celebrating their latest gift, the establishment of the Sarah and Rolando Uziel Laboratory for Metabolic Phenotyping and the Sarah and Rolando Uziel Research Associate Chair. The first incumbent of the chair is Dr. Yael Kuperman, who also heads the Uziel Lab. The new lab will provide state-of-the-art research services and data analysis to about a dozen research groups dealing with type-1 and type-2 diabetes, and also with obesity, immune response, cardiovascular diseases, and cancer.

"There is so much research, so much intelligence, that is part of this new lab and it fills us with energy and makes us proud to be associated with it, and of course with the Weizmann Institute, which we care deeply about," said Mr. Uziel. Mr. Uziel is a past president of the Sephardic Community in Mexico, and the couple has supported many other educational and Jewish causes such as Yad Va'Shem and Keren Kayemet.

About 10 years ago, the couple gave a major gift to support the lab of Prof. Ami Navon of the Department of Biological Regulation.

## American Committee launches NextGen initiative

In April, the American Committee kicked off its NextGen Initiative, aimed at engaging future philanthropic leaders. Held at City Winery in New York, the inaugural NextGen *Science on Tap* brought together young professionals and executives for an evening of science, conversation, and wine tasting.

*L to R: Students Ravit Netzer, Eran Kotler, and Ziv Zwighaft at City Winery in New York City.*

The event featured three outstanding PhD students from the Institute's Feinberg Graduate School who traveled to the U.S. as part of the *Scientists of Tomorrow* tour.

The students enthusiastically discussed their work on subjects varying from cancer to biological clocks to novel proteins, and shared their passion for science. Each student expressed a sense of gratitude for the opportunity to study at the Weizmann Institute and for the values they have learned and acquired. "The quality that scientists need most is persistence," said Ziv Zwighaft of the Department of Biomolecular Sciences, and an ultra-marathon runner. "Things don't always work out, but you have to keep pursuing your questions."

LIFE SCIENCE *Open Day*

**September 8, 2016**

## Open Day for the life sciences

Hundreds of students gathered at The David Lopatie Conference Centre on Sept. 8 for Life Science Open Day, whose purpose is to introduce students to a wide spectrum of research areas from genetics to neurobiology to environmental sciences and cancer research. The event included student talks and poster sessions. Prof. Andrea Manica from the Department of Zoology at the University of Cambridge delivered opening remarks on the ecological approach to human genetics.


*L to R: David Baram, Yael Goren-Wegman, Director of the Israel Friends Association and the Alumni Organization, Itamar Cohen, Yoni Douek, Yonatan Cohen*

# Head start into the start-up world

What makes a good entrepreneur? In an effort to expose Weizmann Institute students to the world of high-tech and biotech entrepreneurship, two Weizmann Institute PhD students have founded and launched a unique program aimed at providing students with knowledge, skills, and the network necessary to launch and develop startup ventures.

WISe, the Weizmann Institute of Science Entrepreneurship Club, was founded earlier this year by Itamar Sivan and Yonatan Cohen, both of whom are studying under the guidance of Prof. Moty Heiblum in the Department of Condensed Matter Physics. The program operates under the auspices of the Feinberg Graduate School and in coordination with the Institute's tech transfer arm, Yeda, and the Alumni Association.

"The underlying desire to make a significant impact, which drives our students to do basic research, is also what drives our alumni to found groundbreaking startups," says Sivan. WISe is a selective program: Of the 120 students who applied, 30 were accepted, mostly PhD students in a diverse set of fields, with many having served in IDF elite units. With alumni involvement, the program consists of talks and seminars, and offers guidance for startup projects.

Alumni Dr. David Baram and Yoni Douek spoke at the Aug. 8 WISe event. Dr. Baram spoke about the four companies he has established, including Emendo, which develops gene editing platforms. Douek described his establishment of Appsee, a start-up that develops in-depth analytical tools for mobile apps that help apps better understand user behavior.


# UK celebrates fundraising target at Global Gathering closing gala

Weizmann UK hosted the 2016 Global Gathering in London in a three-day event that took place in June (see Special Section). While highlights abounded at this unique celebration of science and philanthropy, the closing reception at the V&A Museum and gala dinner at the Natural History Museum were the 'jewels in the crown' from the perspective of UK friends. About 250 Weizmann UK supporters joined the Global Gathering participants, swelling the number of guests for the Inspiring Connections Gala Dinner to almost 500.

In the lead-up to the Global Gathering, Weizmann UK successfully led a $5 million fundraising campaign for the transformation of the Weizmann UK Building for Biocomplexity Research, and the gala dinner celebrated this achievement.

The building provides new space for cancer research, laboratories to advance key investigations into inflammatory diseases such as Crohn's and arthritis, and fertility research. It will be formally inaugurated at the Institute's International Board Meeting in November.

# Wonderful Women in Canada

On May 25, Weizmann Canada's Women and Science committee hosted the third annual Wonderful Women event, presented by TD Bank, at Toronto's Casa Loma.

Committee chair Michele Atlin announced that this was a record-breaking initiative for the Wonderful Women event, as it raised funds to support three grants as part of the Israel National Postdoctoral Award Program for Advancing Women in Science.

More than 300 guests were treated to a cocktail reception followed by a panel discussion. The panel included award-winning author and musician Jann Arden, author and actress Mary Jo Eustace, businesswoman Carrie Kirkman, and Dr. Yifat Merbl of the Department of Immunology. The evening was moderated by well-known journalist and TV personality Dianne Buckner. The panel members shared challenges and triumphs they have experienced in their respective careers. Jann Arden signed copies of her memoir, *Falling Backwards*, and guests enjoyed a delicious dessert reception sponsored by PearTree Financial.

*L to R: Profs. Michal Sharon, Maya Schuldiner, and Nirit Dudovich*

# Motherhood and Science 101

Juggling a demanding career in academic science and raising children is no easy task. So three women scientists at the Weizmann Institute decided not to complain about it and instead do something—and made their lives even busier by creating a course for female students on managing the challenges of parenthood as a principal investigator.

"The idea was: Why don't we give students the benefit of our own experience? We had all wished we had such a course when we were in that situation," says Prof. Michal Sharon of the Department of Biomolecular Sciences. Prof. Sharon initiated and runs the course together with Prof. Maya Schuldiner of the Department of Molecular Genetics, Prof. Nirit Dudovich of the Department of Physics of Complex Systems, and Orit Viterbo, Head of Social Services, with funding from the President's Advisor for Advancing Women in Science, Prof. Daniella Goldfarb.

The course, which consists of six sessions, focuses on practical solutions for managing a career and family, and emphasizes open communication with their advisors, and setting realistic expectations.

"We are part of a culture in which, as women, we are pushed to be perfectionists," says Prof. Schuldiner. "To be the best mother ever. The best scientist ever. "We say, 'You don't have to be best at one or the other. You can be happy about the way you mother and happy about the way that you do science, and you can combine them in a way that is optimal for you and not the outside world.'"

Sometimes, what matters most is simply knowing there are other women in the same position. "When a student feels her situation is impossible, even if it doesn't directly help solve her specific problem for the day, knowing that other women—women who eventually succeeded in their careers—have faced the same difficulties, it gives her some perspective," says Prof. Dudovich.

# New partnership with the Garvan Institute

The Weizmann Institute and the Garvan Institute of Medical Research in Sydney have established a joint center for research in cellular genomics. The Garvan-Weizmann Centre for Cellular Genomics will be housed in the Kinghorn Cancer Centre in Sydney, and will be Australia's only multidisciplinary facility for cellular genomics: the study of the molecular genetic states of thousands of individual cells. The center's mission is to help researchers develop a detailed understanding of how the genomes and gene expression programs of individual cells in the brain, the immune system, and other organs change over the course of a lifetime; how cancers, autoimmune diseases, dementia and other conditions develop; and how to design new strategies for prevention and treatment.

## Fifth Thompson conference on cancer research

The Weizmann Institute hosted the fifth annual Thompson Family Foundation Conference on campus on Aug. 15 and 16 as part of the foundation's efforts to advance collaborative research between the Institute and Memorial Sloan Kettering Cancer Center (MSKCC) in New York.

"Every single scientific group that we support is defined by excellence... and excellence is our guide for giving," said Amanda Reigel (pictured above), who serves as President of the foundation. Speaking to the scientists and physicians in the room, she said, "Continue to pursue excellence and a cure for cancer," said Ms. Reigel. Ms. Reigel is the daughter of the late Wade Thompson, who established the foundation before his death from cancer in 2009.

The event was led by Prof. Avigdor Scherz of the Department of Plant and Environmental Sciences and Dr. Jonathan Coleman, a urologic surgeon at MSKCC. Dr. Coleman led U.S. efforts in multi-center clinical trials for early-stage prostate cancer based on drug therapy developed by Prof. Scherz and Prof. Yoram Salomon of the Department of Biological Regulation with STEBA Biotech, a collaboration funded by the foundation. Dr. Coleman is currently leading clinical trials of the therapy for advanced prostate cancer, bladder cancer, gastroesophageal cancer, and breast cancer.

## Lighting the way with Sparks of Science

Two dozen students graduated in June from the Sparks of Science Program in Memory of Moshe Pergament, as the program completed its 15th year. To date, it boasts about 300 alumni. At the heart of the Sparks of Science Program in Memory of Moshe Pergament is the belief that offering exposure to science at a young age could lead to future success—not just in science, but in any path ahead.

The program brings together youth from 9th through 12th grades from Rehovot and a dozen municipalities in the area. Once a week, over the course of four years, participants take part in activities in biology, chemistry, computer science, and physics at the Davidson Institute of Science Education. Students also receive enrichment in English and math and participate in sessions on empowerment, decision-making, and time management.

The lion's share of the budget for Sparks of Science comes from the support of Hana and Irving Pergament, a gift they made to memorialize their son Moshe. The Pergaments, Israelis who are long-time residents of New York, visit Israel every June to take part in the commencement ceremony. "In the first year, the students arrive with only a vague idea about their future," said Mr. Pergament. "Four years later, they have a path and knowledge, and they want to pursue academic degrees. They are also better integrated into Israeli society."

*Sparks administrator Freihut Belay-Tadela and Hana Pergament*

The roots of Celia Zwillenberg-Fridman's giving to the Weizmann Institute are literally in the soil.

Born in Argentina to a father who was an agronomist on a Jewish agricultural colony, Celia grew up with an appreciation for science and went on to receive a PhD in biochemistry. She and her siblings were thus part of a small but intriguing piece of Jewish history, having grown up on a Baron de Hirsch colony in rural Argentina, where their father worked as an instructor. The colony was one of several established by that German Jewish philanthropist, who founded the Jewish Colonization Association just prior to turn of the 20th century for the purpose of resettling Jews fleeing persecution in Imperial Russia.

Like other children who grew up in the Baron de Hirsch colonies, they were taught a love for the land and a love of Israel. Two of Celia's siblings made aliya and were co-founders of Kibbutz Gazit in the Galilee, and after Celia completed her PhD at the National University of La Plata (Buenos Aires), she moved to Israel in 1963.

## Grapefruits and soybeans

Her first job in Israel was in a hematology lab at Afula Hospital, and her second at the Volcani Institute, the Israeli government's agricultural research facility, where she researched the composition of grapefruits using a method called chromatography. Then, she got what she called her "dream job," in the lab of Prof. Nathan Sharon at the Weizmann Institute, in what was then the Department of Biophysics. "In Argentina, as a girl, I read a publication about Israel in which the Weizmann Institute was mentioned, and I decided then that it was my dream to work there," recalls Dr. Zwillenberg. "I was thrilled when it actually happened."

In Prof. Sharon's lab in the Ullman Building, she studied the amino acid composition of soybeans. She published several journal articles with Prof. Sharon and Prof. Ephraim Katzir, who headed the Department of

# Profile of a Pair

54–55

# Dr. Celia Zwillenberg-Fridman and Dr. Kobi Abramson

*Dr. Zwillenberg-Fridman as a young scientist in the lab of the late Prof. Nathan Sharon*

*From Weizmann scientist to Weizmann donor, the closure of a circle*

Biophysics (and later became Israel's fourth President).

"I worked there for six years, and they were unforgettable ones," she recalls. "Everyone in the lab welcomed me into their families, hosted me at their homes, taught me Hebrew... I am forever grateful for this, and for all the help I received as a new immigrant in Israel. So when I was able to give back, I decided to give to young scientists at the Weizmann Institute."

It was at the Institute that she met her husband, Lutz, a Swiss scientist who came to the Institute as a visiting scientist, where he studied fish. And thus her time in Israel came to an end: She moved back to Switzerland with him and settled in Bern, where she lives today. She worked in his lab at the University of Bern where he specialized in electron microscopy and later established a private lab. He published a book on the relationship between science and religion, and, together with Celia, organized public lectures on Judaism. The couple had two daughters, Daphna and Tamara. Celia missed Israel, but she threw herself into her work, her family life, and became (and is still) very active in the Swiss Jewish community.

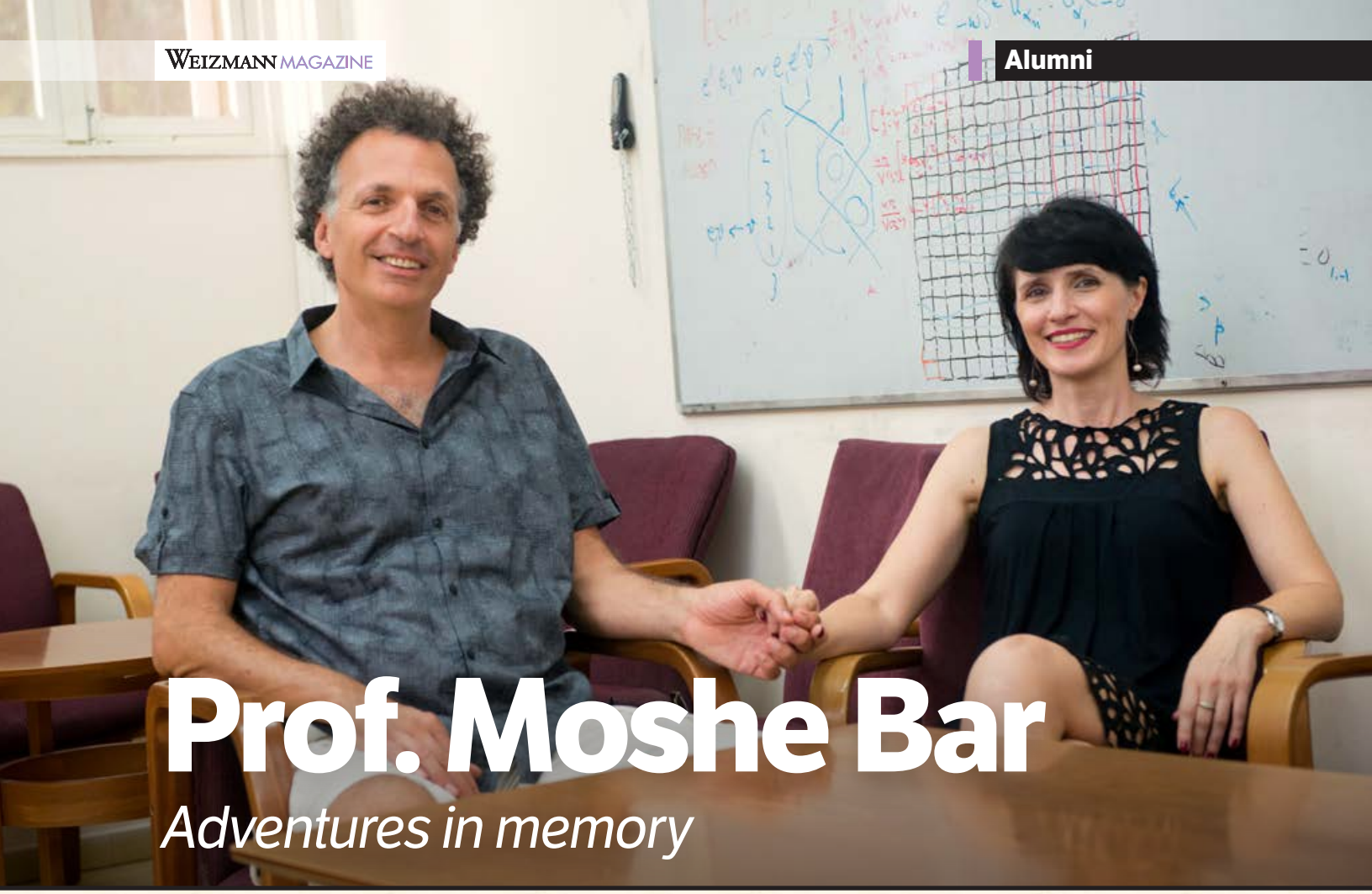
## Investing in the next generation

In 2011, the couple established the Dr. Celia Zwillenberg-Fridman and Dr. Lutz Zwillenberg Career Development Chair, with Dr. Kobi Abramson of the Department of Immunology as the first incumbent (pictured with her). Lutz was too ill to travel to Israel for the dedication ceremony, and died later that year. The gift, says Celia, was a way to pay tribute to the Weizmann Institute and at the same time honor the place where she and Lutz first met.

Dr. Abramson, who made aliya from Prague, was a "perfect match," says Celia, because he was a young immigrant, and because his area of study intrigues her: He studies the molecular and cellular mechanisms that control the establishment of immunological tolerance, a process in which the immune system "learns" to recognize and tolerate the body's own components.

Last year, Celia made another major gift to the Weizmann Institute, this time for start-up funds for Dr. Yifat Merbl, also of the Department of Immunology. Dr. Merbl's research explores the many modifications that proteins undergo in the human body. She developed a high-throughput system to monitor post-translational changes in thousands of proteins in parallel, under conditions close to those of the complex cellular environment. These changes are instrumental to the activity of proteins, and revealing the regulatory code that controls altered protein function is key to understanding the dynamic regulation of cells in health and disease.

"Celia is a wonderful woman and a scientist who cares about ensuring that the next generation of Israeli scientists has the tools they need to succeed in their job, and I am incredibly grateful for her support of my chair," says Dr. Abramson. "It is an honor to hold the chair that she and Lutz created together, here at Weizmann, where they met and started their lives together—as scientists and as husband and wife."



# Prof. Moshe Bar

## *Adventures in memory*

A conversation with cognitive neuroscientist and Weizmann Institute alumnus Prof. Moshe Bar offers a real-time encounter with the subject he examines in his 2011 book, *Predictions in the Brain* (Oxford University Press). A multi-disciplinary look at how the "nuts and bolts" of memory support whole-brain experiences, the book is a collection of essays describing the complex neural activity required for a person to recall his or her past, process the present, and imagine the future.

"Thinking back on my early days—a bachelor's in electrical engineering, followed by my time at the Weizmann Institute studying for my masters in computer science and applied math—I would never have predicted that I'd end up in neuroscience," says Prof. Bar, who today heads Bar-Ilan University's Gonda Multidisciplinary Brain Research Center. "But the path you take informs your thinking. My academic training combined biomedical engineering, math, medicine and psychology—a combination of influences that led to a wide open, and not-very-traditional approach to neuroscience. Maybe it's because I'm naturally distractible; my curiosity led me in many different directions."

Born in the small town of Dimona in the central Negev, Prof. Bar attended high school in Tel Aviv, then returned south to attend Ben-Gurion University. It was there—a half hour's drive from his childhood home—that he first encountered the subject that would send him around the world and back again.

As an undergrad majoring in image processing and biomedical engineering, Prof. Bar was introduced to tools that allow scientists to observe and quantify biological processes. Later, in parallel with his service in the Israel Air Force, he completed his masters at the Weizmann Institute, working on projects relating to human vision and computer vision in the lab of Prof. Shimon Ullman of the Department of Computer Science and Applied Mathematics. Prof. Bar fondly recalls his training under Prof. Ullman—a world leader in the field—calling him "an exceptionally generous mentor who is still a major inspiration to me."

Despite his busy schedule, Prof. Bar found time to be inspired by someone else at the Institute—the graduate student, Maria Lando, who would eventually become his wife.

# Alumni




"When I first saw Maria, in the Ziskind mathematics building, I literally fell off my chair," Prof. Bar says. Maria's post-Weizmann career led her to Hollywood, where she used her math skills to design spectacular special effects for films including *Air Force One* and *Godzilla*. Later, she also launched *themathmom.com*, a website that provides creative resources for parents who want to integrate mathematics education into daily life.

The young couple's Los Angeles sojourn began when Prof. Bar was accepted into a doctoral program at the University of Southern California—a move he credits to the many hours he and Maria spent in the Weizmann Institute's Charles Clore International House, studying together for his qualifying exams.

As a PhD candidate, he trained under Prof. Irving Biederman, a pioneer of theories surrounding the psychological and neurological basis of vision. Later, for his postdoctoral research at Harvard University, the family relocated to Boston. There, he worked with Prof. Daniel Schacter, a noted psychologist whose research focuses on the psychological and biological aspects of human memory and amnesia. He also trained with Prof. Roger Tootell, one of the first scientists to use fMRI to study human visual perception.

After his postdoc, Prof. Bar attained a joint faculty appointment at Harvard Medical School and Massachusetts General Hospital. During that time, his growing body of published work—elucidating how the brain extracts and uses contextual information to generate predictions and guide cognition—led to professional offers from universities all over the world. Eventually, however, the Bar family decided it was time to come home. With their two older kids, they arrived in Israel in time for the birth of their third child, who is now five years old.

"We were happy in Boston, but we wanted to be closer to the extended family, and also wanted to establish a healthy balance in life," he says. On a recent birthday—his 50th—he illustrated the balance he strives for by sharing with guests a famous Hassidic story about the two notes people should always carry in their pockets, one saying "I am as worthless as dust," and the other saying, "The entire world was created for me."

"In neuroscience, the ability to hold two opposing convictions is called bi-stable perception," Prof. Bar says. "It also helps sum up my experience, all those years ago, as a student at the Institute. On the one hand, you feel the entitlement that comes from being, in a sense, on the very top of the scientific world. On the other hand, living in a community with so many brilliant people keeps you humble. This is certainly not the only lesson I learned from the Weizmann Institute, but it's one of the most valuable."

# Ravit Netzer

*Designing proteins to catch proteins*

# Students



In the long-time tradition of setting a thief to catch a thief, Ravit Netzer is designing proteins to catch proteins.

"Proteins are involved in every aspect of life," she says. "They convert food into energy. They signal light, taste and smell to the brain. Our enzymes and antibodies are categories of protein. And illnesses from cancer to diabetes to dementia are essentially protein malfunctions. If we can design proteins that recognize the right targets and ignore other molecules, we can create new and very specific therapies."

Netzer, 31, is a doctoral student at the Weizmann Institute's Feinberg Graduate School, and her fascination with science was kindled under the massive steel tanks of the Zohar Dalia soap and detergent factory on Kibbutz Dalia, near Haifa, where she was born. "Dalia built a soaping kettle, which has grown into Israel's largest soap and detergent developer and manufacturer," she says. "As a child, I was endlessly curious about what went on inside those tanks."

When she took a job during her summer vacation at the plant after 9th grade, she found out—and her curiosity only grew from there. "I worked in the factory's chemistry lab, helping test soaps and detergents, and I loved every moment," she smiles. She chose chemistry as a high school elective after that summer, and studied both chemistry and biology at the Hebrew University of Jerusalem for her bachelor's degree. "I was fascinated by their interface — by the chemical processes that build the human body," she says.

During her service in the Israel Defense Forces, she discovered she enjoyed research. As an Intelligence Corps soldier and then an officer, she assembled disparate information into a bigger picture. "I wanted to do graduate study, and kept hearing that the Weizmann Institute is the best place for the quantitative chemical and biological research that interests me."

Rotating in different Institute labs, Netzer encountered the field of computational protein design in the Department of Biomolecular Sciences in Dr. Sarel Fleishman's lab. She had no experience with computation, but quickly learned it was essential to designing proteins. "Even in moderate-sized proteins, there are astronomically large numbers of amino acid sequences," she says. "Evaluating the quality of different sequences is a job for the computer."

*Ravit Netzer's interest in science began as a child on the kibbutz, where she saw the production of soap and detergents.*

Netzer joined the lab for her MSc, and is now working toward a PhD, aiming to design proteins that recognize and correct specific problems. "Existing pharmaceuticals that target malfunctioning proteins have mostly been developed by trial and error," she says. "We're trying to understand a protein's basic properties and the form and behavior they give it. The more we understand, the better able we'll be to make it do what we want."

Gifted not only scientifically, but also with the ability to make her abstruse research comprehensible to lay audiences, Netzer is a regular on the *Science On Tap* circuit — a Weizmann Institute program in which its scientists describe their work in Tel Aviv bars to a relaxed audience with beers in hand. *Science on Tap* gives her 45 minutes to describe her niche subject. An Institute-organized delegation called *Scientists of Tomorrow* took her and two fellow doctoral students to meet Institute supporters and prospects in Florida and New York in April. "Their enthusiasm blew me away," she says.

## Kobi Abramson

- Ruth and Samuel David Gameroff Family Foundation
- The Richard F. Goodman Yale/Weizmann Exchange Program
- Estate of Raymond Lapon
- Rising Tide Foundation
- Sy Syms Foundation
- Wohl Biology Endowment Fund

- Dr. Abramson is the incumbent of the Dr. Celia Zwillenberg-Fridman and Dr. Lutz Zwillenberg Career Development Chair

## Ronen Alon

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- Prof. Alon is the incumbent of the Linda Jacobs Professorial Chair in Immune and Stem Cell Research

## Ido Amit

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- Swiss Society of Friends of the Weizmann Institute of Science

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## Elisabetta Boaretto

- Dangoor Accelerator Mass Spectrometer

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## Zelig Eshhar

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## David Harel

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- The Willner Family Leadership Institute for the Weizmann Institute of Science

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- The Sarah and Rolando Uziel Laboratory for Metabolic Phenotyping

- Dr. Kuperman is the incumbent of the Sarah and Rolando Uziel Research Associate Chair

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- Estate of Flora Frank

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## Noam Sobel

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- The late H. Thomas Beck
- The Nella and Leon Benoziyo Center for Neurosciences, which he heads
- The Carl and Micaela Einhorn-Dominic Institute for Brain Research, which he heads
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- The Schwartz/Reisman Institute for Theoretical Physics which he heads

- Prof. Waxman is the incumbent of the Max Planck Professorial Chair of Quantum Physics

## Stephen Weiner

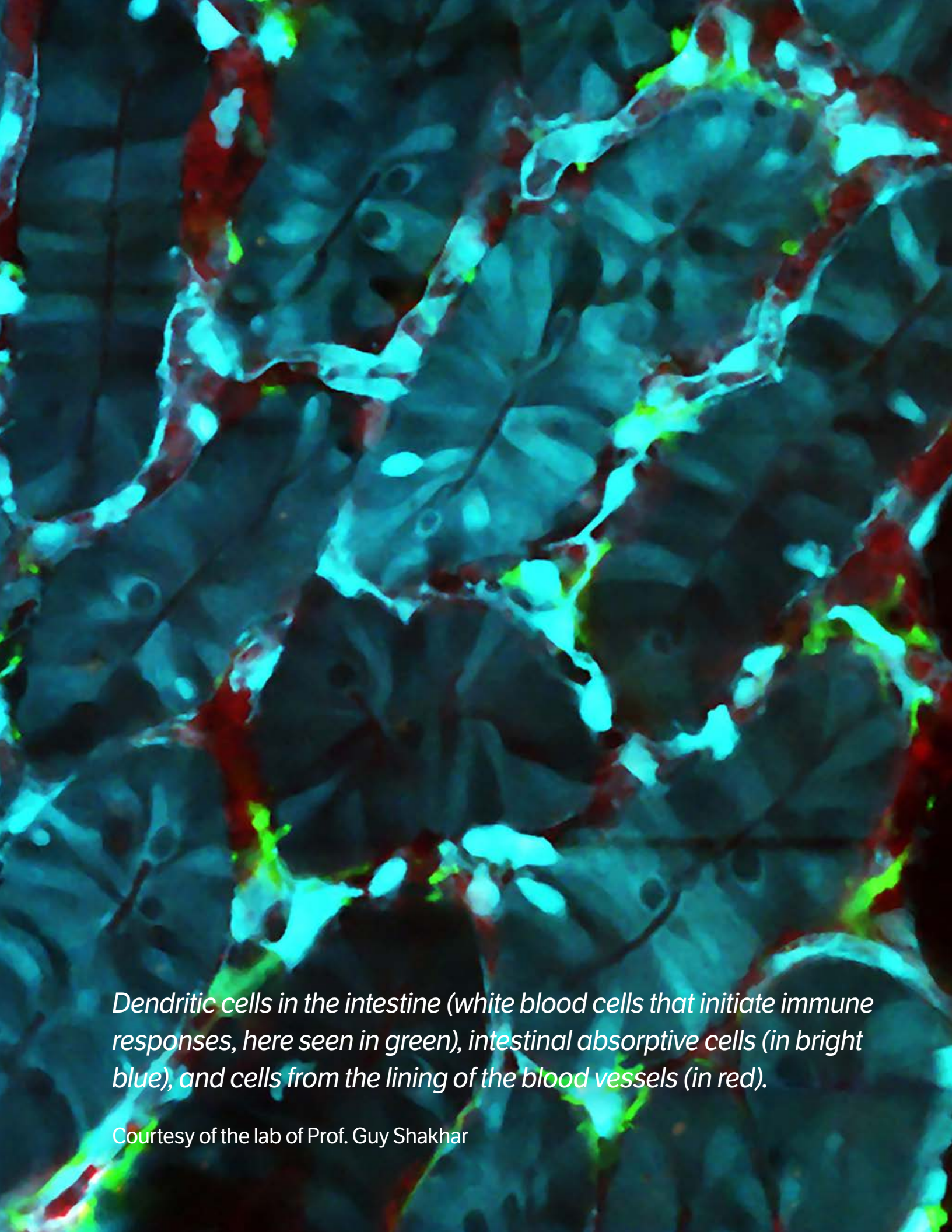
- Dangoor Accelerator Mass Spectrometer Laboratory
- Helen and Martin Kimmel Center for Archaeological Science which he heads
- Estate of George & Beatrice F. Schwartzman
- Prof. Weiner is the incumbent of the Dr. Walter and Dr. Trude Borchardt Professorial Chair in Structural Biology

# Immunity

/ih-**myoo**-ni-tee/

*noun*

The condition that permits either natural or acquired resistance to disease.



*Dendritic cells in the intestine (white blood cells that initiate immune responses, here seen in green), intestinal absorptive cells (in bright blue), and cells from the lining of the blood vessels (in red).*

Courtesy of the lab of Prof. Guy Shakhar