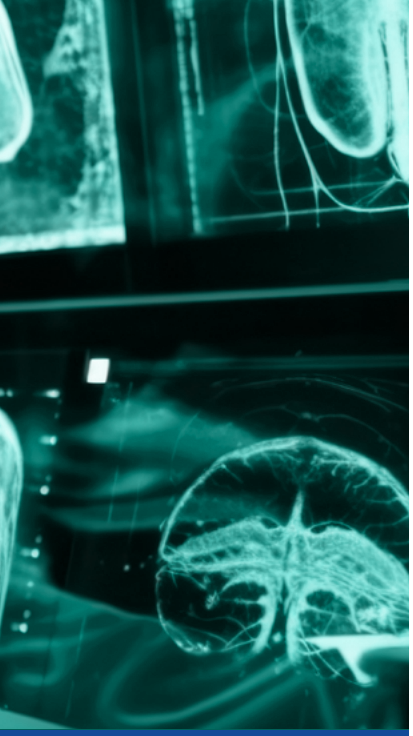

AMERICAN TECHNION SOCIETY

2023

From **Visionary Education** to a **World** of **Impact**

The Allen and Jewel Prince Center for Neurodegenerative Disorders of the Brain

Produced in partnership with the Technion Division of Public Affairs and Resource Development

The American Technion Society

The American Technion Society supports visionary education and world-changing impact through the Technion - Israel Institute of Technology. Based in New York City, we represent thousands of U.S. donors, alumni, and stakeholders who invest in the Technion's growth and innovation to advance critical research and technologies that serve the State of Israel and the global good. For 80 years, our nationwide supporter network has funded Technion scholarships, research, labs, and facilities that have helped deliver world-changing contributions and extend Technion education to campuses in three countries.

For more than a century, the Technion - Israel Institute of Technology has pioneered in science and technology education and delivered world-changing impact. Proudly a global university, the Technion has long leveraged boundary-crossing collaborations to advance breakthrough research and technologies. Now with a presence in three countries, the Technion will prepare the next generation of global innovators. Technion people, ideas, and inventions make immeasurable contributions to the world, innovating in fields from cancer research and sustainable energy to quantum computing and computer science to do good around the world.

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The Prince Center

Exploring the Mysteries of Brain Function and Dysfunction

Established in 2012, the Allen and Jewel Prince Center for Neurodegenerative Disorders of the Brain is affiliated with the Technion's Ruth and Bruce Rappaport Faculty of Medicine. Led by Professor Jackie Schiller, the Prince Center is home to 12 principal investigators – all embarked on an extraordinary journey of discovery to unlock the secrets of the human brain, how this mysterious organ maintains itself, and how and why critical functions can be lost. Playing a key role in the Technion's Human Health Initiative – one of the university's central pillars for research in the 21st century – this extremely talented group of thinkers encompasses both early-career scientists and world-renowned researchers.

This year's Prince Center report spotlights a range of advances in brain research achieved by Prince Center faculty members over the past year. These include the critical role of proteins on brain cell structure and function; a potential link between brain stimulation and heart health following a heart attack; and the negative effects that certain genetic mutations can have on learning and memory.

The Technion once again offers thanks to Allen and Jewel Prince, whose generous gift led to the establishment of the Allen and Jewel Prince Center for Neurodegenerative Disorders of the Brain.

Professor Jackie Schiller, Prince Center director, with research students in her lab at the Technion - Israel Institute of Technology.

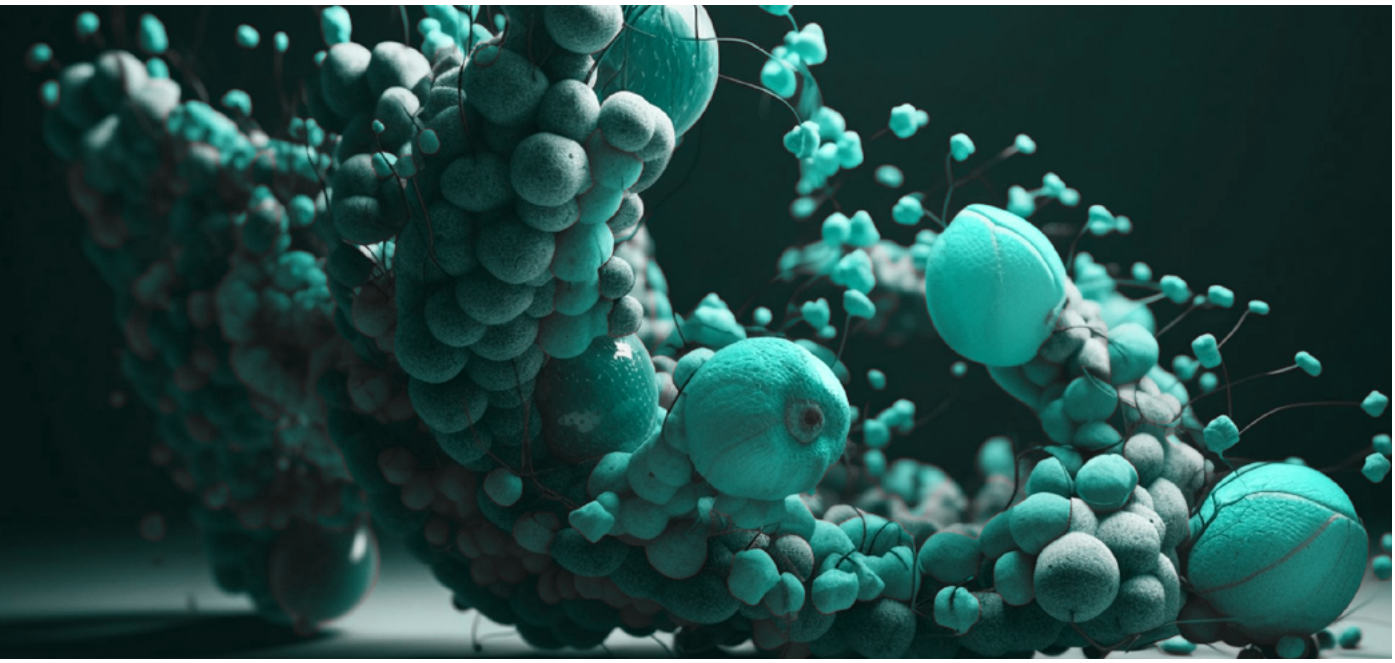
The Prince Center Director

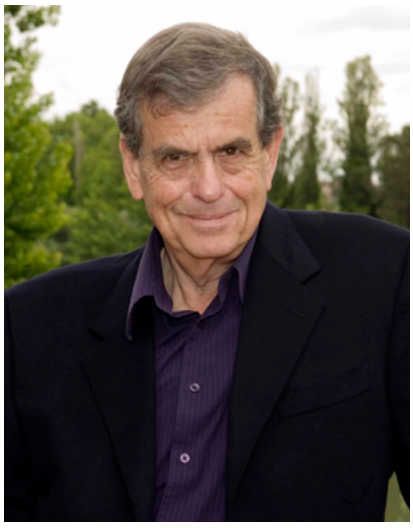
Elucidating the Role of Individual Neurons in Brain Activity

Professor Jackie Schiller

Professor Jackie Schiller holds the Lily and Silvian Marcus Chair in Life Science, is head of the Department of Neuroscience in the Technion's Ruth and Bruce Rappaport Faculty of Medicine, and is director of the Allen and Jewel Prince Center for Neurodegenerative Disorders of the Brain. She is also a researcher in the Russell Berrie Nanotechnology Institute. Prof. Schiller's work in the Rappaport Faculty of Medicine and the Prince Center seeks to understand the brain's largest and most complex structure, the cerebral cortex, and its links to Parkinson's disease, epilepsy, autism, and more.

Professor Schiller and her team continue to elucidate their landmark finding that computation in the brain occurs not just in the interactions among multiple nerve cells but also within each individual neuron. In effect, each of these microscopic cells operates not like a simple switch but rather as a complex calculating machine, akin to a tiny biological computer. Each cell performs a calculation that influences where its signal is subsequently forwarded. The neurons to which Prof. Schiller's team directed their attention play a key role in movement. The insights they have uncovered as a result of their study could provide a better understanding of Parkinson's disease, in which the neurons' abilities to perform computations is reduced.





Distinguished Professor
Aaron Ciechanover

Distinguished University Professor
Aaron Ciechanover

Distinguished Prof. Aaron Ciechanover received the 2004 Nobel Prize in chemistry for his studies of ubiquitin, a protein that attaches itself to unwanted or damaged proteins and oversees their breakdown into smaller pieces – a key biological process in all animals and plants. That research has led to the development of several anti-cancer drugs including Velcade® and an entire family of immunomodulatory drugs. As a senior member of the Prince Center, Prof. Ciechanover is investigating how the ubiquitin system can be used to get a better understanding of how proteins aggregate in cells and lead to neurodegeneration in Huntington's disease, as well as how protein aggregation may influence the pathology of Alzheimer's disease.

Overview of Recent Prince Center Research

The Impact of Proteins on the Brain

Associate Professor **Simone Engelender**	Preventing the Accumulation of Proteins Triggering Parkinson's Disease
Associate Professor **Reut Shalgi**	A Closer Look at Protein Clumping in Neurodegenerative Diseases
Professor **Herman Wolosker**	Preventing Neurodegeneration with Amino Acids
Professor **Noam Ziv**	Brain Cells Degrade When Proteins Are Scarce

Associate Professor

Simone Engelender

Preventing the Accumulation of Proteins Triggering Parkinson's Disease

A team led by Associate Professor Simone Engelender is further studying how removing unwanted protein deposits might be a way to treat neurodegenerative diseases. Many such diseases involve the accumulation of protein deposits in the brain that arise when structures called neurofibrillary tangles start to form within nerve cells. In particular, Assoc. Prof. Engelender's team has identified a set of chemical processes that are known to contribute to the buildup of proteins, and have suggested how these processes might be reduced or prevented in the brain. For example, one particular protein, alpha-synuclein, is thought to play a role in the development of Alzheimer's, Parkinson's (marked by stiffness, slowness, and tremor), amyotrophic lateral sclerosis (involving muscle weakness), Huntington's, and frontotemporal lobal degeneration. The team's strategy – which involves eliminating the protein deposits by enhancing the rate at which those deposits degrade – could in turn prevent the proteins from causing brain cells to misfire and die.

Associate Professor

Reut Shalgi

A Closer Look at Protein Clumping in Neurodegenerative Diseases

Associate Professor Reut Shalgi's team is advancing its previously reported discovery: brain cells have the ability to prevent protein clumps that cause neurodegeneration. But when those cells fail to do so, conditions like Huntington's disease and ALS can develop. Asst. Prof. Shalgi's team examined 66 types of molecular "chaperones" – which are key to avoiding protein clumping – in brain cells. They found that in Huntington's disease, brain cells activated the wrong chaperones to clear the proteins; in ALS, the brain cells didn't activate any chaperones at all. As the team noted, brain cells must know how to harness chaperones properly to resolve the problem. These findings could point toward future treatments for Huntington's and ALS.

Professor

Herman Wolosker

Preventing Neurodegeneration with Amino Acids

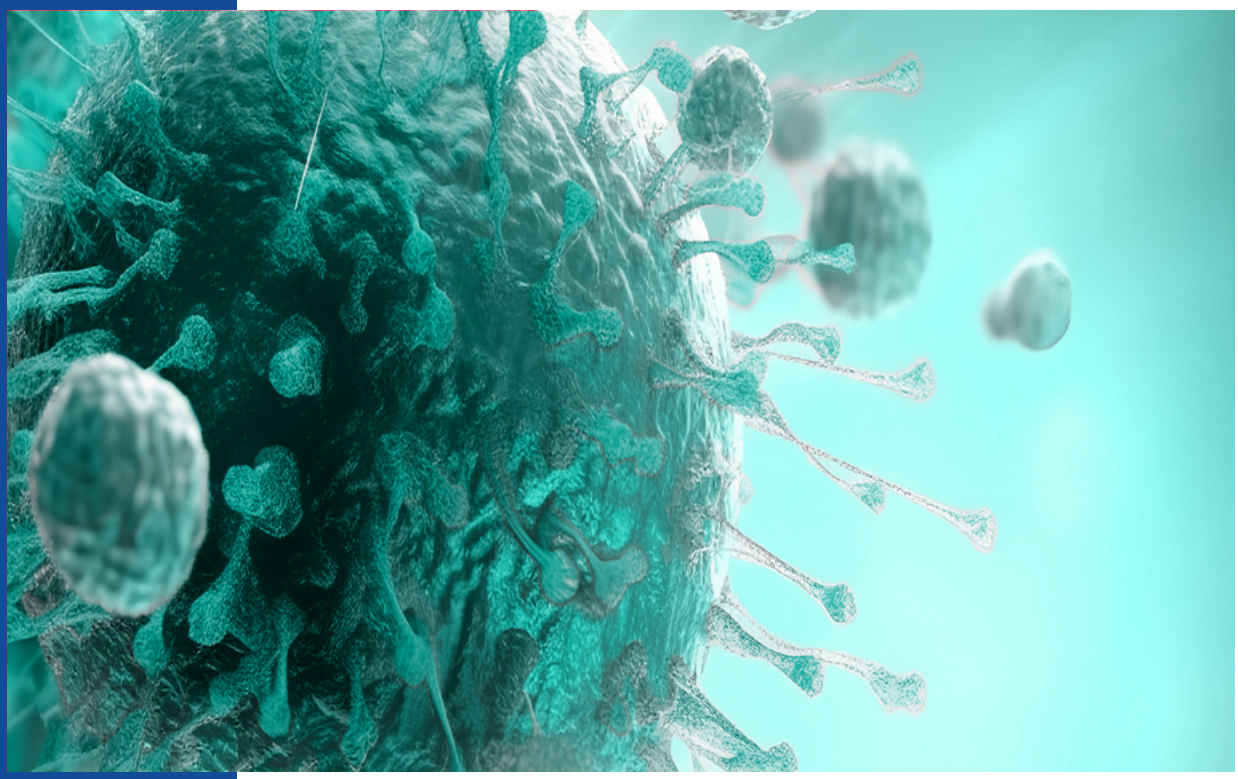
Sometimes, gene variants – also known as mutations – prevent one or more proteins in the body from working properly. By changing a gene's instructions for making a protein, a variant can cause a protein to malfunction. **Professor Herman Wolosker** and his team have found that children with a mutation in a specific protein tend to have severely stunted brain growth. This mutation is more common among Ashkenazi Jews and can cause lifelong disabilities that make simple movements challenging. Now, by studying mice with the same mutation found in humans, Prof. Wolosker's team has discovered that the protein in question transfers an amino acid named serine into the brain through the blood–brain barrier, a structure that keeps harmful substances out of the brain. Without this amino acid, the mice suffered from neurodegeneration and motor dysfunction. Encouragingly, Prof. Wolosker found that giving the mice extra serine – which can be found in over-the-counter supplements – prevented the brain growth problems and other negative effects of the mutation. This means that a simple treatment could potentially help children with this condition avoid the disabilities they might otherwise experience. The research team is now investigating if this form of treatment can also impact other types of neurodegeneration.

Professor

Noam Ziv

Brain Cells Degrade When Proteins Are Scarce

The health of every cell in the human body, including the nerve cells (neurons) in our brains, depends on the availability of a continuous supply of fresh proteins. Continuous protein renewal is vital for maintaining the structural integrity and functional properties of cells in the brain. As neurons are generally not replaced over one's lifetime, the viability of the brain is highly dependent on the continual production of proteins and the appropriate disposal of damaged ones. **Professor Noam Ziv** and his colleagues are focused on the supply and demand of the proteins that keep our brain cells operating normally. In one study, Prof. Ziv's lab used a technique called mass spectrometry to measure the properties of neuronal proteins, and how the lifetimes of neurons are affected when the supply of fresh proteins is limited. They found that acute disruptions in the supply of new proteins can lead to the destabilization and loss of connections between nerve cells in the brain, and an impairment of these cells' ability to consume oxygen, long before obvious cell death is observed. This complements a separate study Prof. Ziv is conducting on the protein huntingtin, the culprit in Huntington's disease – an inherited disorder that causes nerve cells in parts of the brain to break down and die, resulting in a range of motion disorders.



The Brain, the Immune System, and Heart Health

Associate Professor
Asya Rolls

Finding a Connection Between the Brain and the Immune System

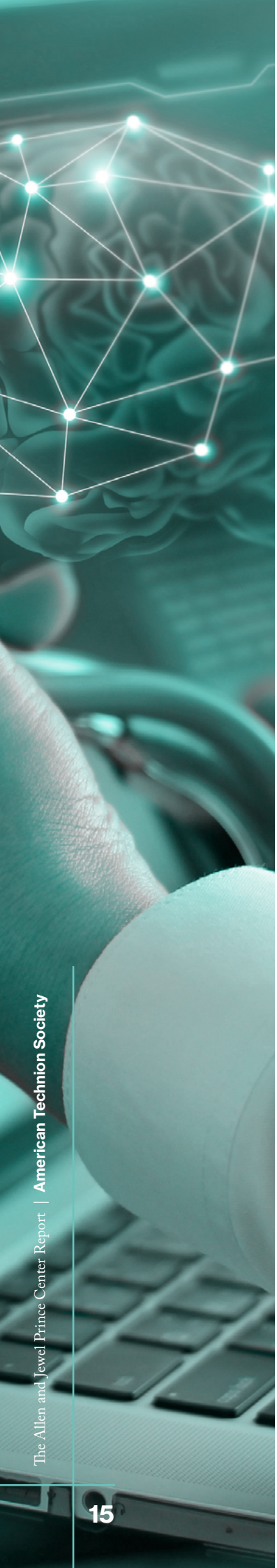
Can Brain Reward Stimulation Affect Human Health?

Associate Professor

Asya Rolls

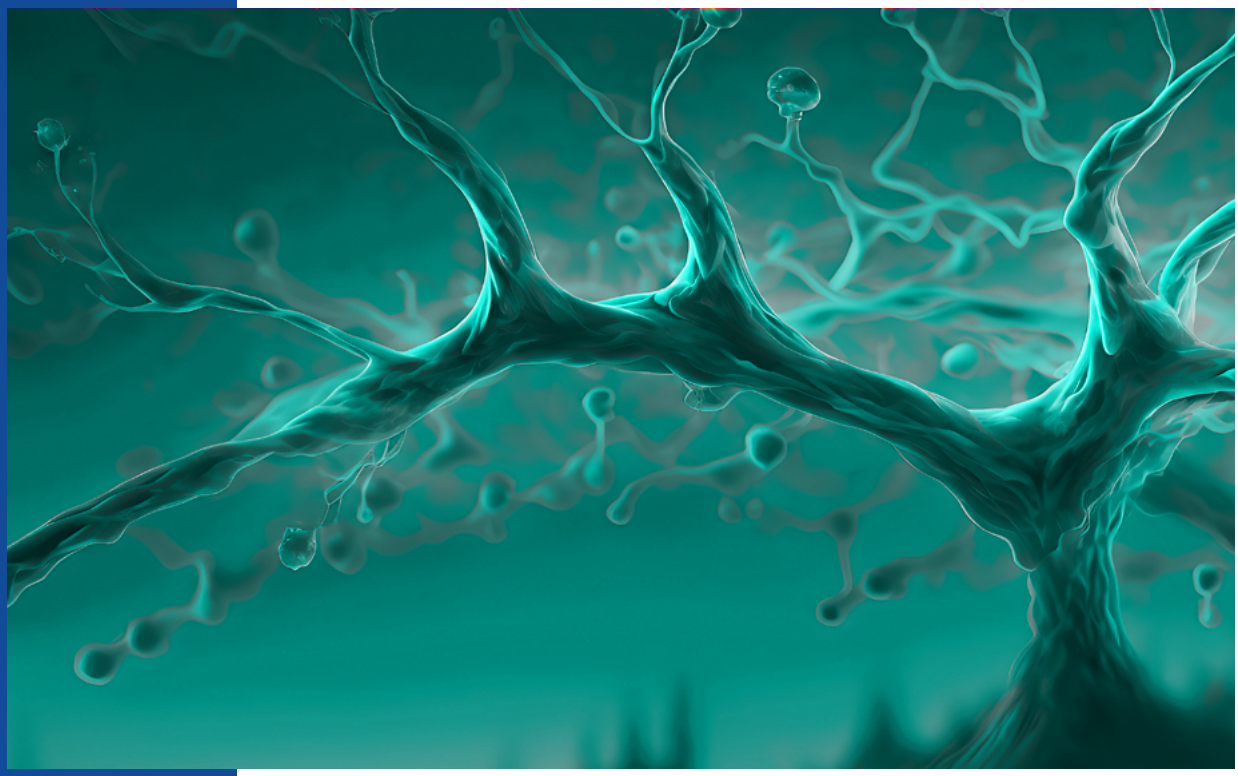
Finding a Connection Between the Brain and the Immune System

A major study by **Associate Professor Asya Rolls** and M.D./Ph.D. student Tamar Koren has attracted additional attention in publications ranging from *Nature* to *Scientific American*. The researchers showed brain activation can trigger and suppress physical symptoms such as inflammation, a key facet of many diseases. Assoc. Prof. Rolls and her team triggered inflammation in mice and identified cells in rodent brains showing increased activity during the inflammation. The researchers then triggered the same brain cells and found inflammation re-emerging without any external stimulus. It was as if "remembering" the inflammation was enough to have it recur physically. The study may lead to therapies for chronic inflammation.



Can Brain Reward Stimulation Affect Heart Health?

In another study, Assoc. Prof. Rolls, working with Ph.D. student Hedva Haykin, is investigating a fascinating question: Can stimulation of a brain region that is involved in positive emotion and motivation help influence how the heart heals? As reported in a *Nature* article in March 2023, the team examined samples of heart tissue from mice that had experienced heart attacks. Some of the mice had received stimulation of their brains' reward centers; the other mice had not. The team observed that those mice who had received stimulation of their brain reward centers seemed to have undergone immune changes that contributed to the reduction of scar tissue in their heart samples. In other words, the *emotional* effects resulting from stimulating the mice's reward centers had a beneficial *physical* effect on how their hearts healed. This raises the exciting possibility that a similar effect might be possible to observe and measure in human patients. Can a positive mindset lead to better outcomes in those with cardiovascular disease? Further research in Assoc. Prof. Rolls' lab will seek to determine if the mechanisms responsible for their striking finding in mice are also present in humans.



Genetic Mutations, Spatial Learning, and Memory

Assistant Professor
Shai Berlin

Finding New Links Between Genetic Mutations and Brain Function

Associate Professor
Dori Derdikman

Studying Loss of Spatial Learning and Memory in Alzheimer's Disease

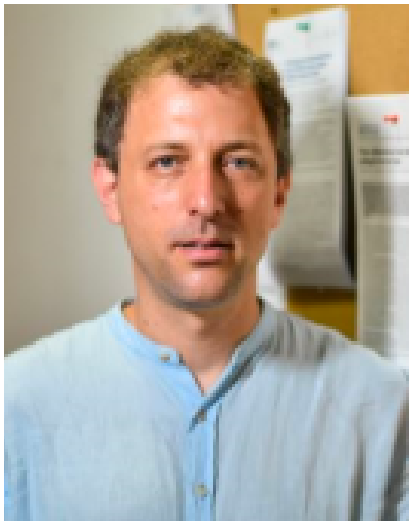
Assistant Professor

Shai Berlin

Finding New Links Between Genetic Mutations and Brain Function

Assistant Professor Shai Berlin is focused on developing genetic and chemical tools to study the healthy and diseased brain. In a study published in *eLife* in 2021, Asst. Prof. Berlin and his colleagues studied two toddlers with mutations occurring within a particular class of genes known as *GRIN* genes. These particular genes oversee multiple functions within the brain, including various aspects of learning and memory.

Mutations within these genes often lead to devastating brain disorders and diseases that alter the development of the brain and cause serious problems such as intellectual disability, hypotonia, and epilepsy. Termed GRINopathies, no treatments for these disorders are currently available. In a follow-up study in 2023, Asst. Prof. Berlin and his team looked more closely at how GRINopathies affect certain receptors in the brain. They discovered that the function of some receptors could be partially restored by a common neurosteroid drug known as pregnenolone sulfate. The investigations led by Asst. Prof. Berlin and his team have contributed to ongoing efforts to understand the pathophysiology of GRINopathies as well as toward the development of potential treatments.



Associate Professor

Dori Derdikman

Studying Loss of Spatial Learning and Memory in Alzheimer's Disease

This past year, **Associate Professor Dori Derdikman** continued his ongoing investigations into the brain mechanisms that continue to fail during the progression of Alzheimer's disease, marked primarily by memory loss and confusion. He has focused his attention on how our sense of orientation within space and time can be impaired in Alzheimer's patients, as well as the role that a particular region of the brain, known as the hippocampus, plays in this process. Using cutting-edge technology, Assoc. Prof. Derdikman and his team have monitored the brain activity of hundreds of nerve cells simultaneously, to learn how these cells influence (or hinder) spatial learning and memory. Assoc. Prof. Derdikman anticipates that his research might someday improve the targeting of therapeutics to address the symptoms of Alzheimer's disease.

L-R / Boaz Golany, Allen Prince, Jewel Prince, Lena Lavie, Prof. Peretz Lavie, Prof. Uri Sivan

About the Prince Family

Allen and Jewel Prince are passionate and committed supporters of the Technion, its vital mission to secure the growth and development of the State of Israel, and the technologies it generates that help people all over the world. They have participated in several American Technion Society missions to the Technion. Members of the ATS South Palm Beach (Fla.) chapter, they have hosted numerous parlor meetings in their home to share their enthusiasm and to introduce others to the Technion. In addition to establishing the Prince Center, they have established the Allen and Jewel Prince Molecular Immunology Research Laboratory Complex, including the complete infrastructure renovation of an entire floor of the Ruth and Bruce Rappaport Faculty of Medicine.

The Allen and Jewel Prince Center for Neurodegenerative Disorders of the Brain

The Allen and Jewel Prince Center for Neurodegenerative Disorders of the Brain continues to distinguish itself as a preeminent site for discovery during an era in which understanding the fundamental science and treatment of brain disorders is ever more important. As a crucial component of the Technion's Human Health Initiative – and a keystone of Technion prestige as the university looks forward to celebrating its Centennial in 2024 – the research conducted at the Prince Center is likely to benefit a wide range of stakeholders in the years and decades to come.

For more information on the Allen and Jewel Prince Center for Neurodegenerative Disorders of the Brain, please click here or email info@ats.org. To make a gift to the Technion, please visit ats.org/donate.

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