Prusiner-Abramsky Research Awards

Former Recipients 2013

Prof. **ALEXANDER LOSSOS**
Department of Neurology
Hebrew University-Hadassah Medical School
Diagnosis and treatment of adult polyglucosan body disease

Dr. **HANNA ROSENMANN**
Department of Neurology
Hebrew University-Hadassah Medical School
Alzheimer's disease and tauopathies - improved animal models, pathogenesis and therapeutic approaches

Dr. **SARA EYAL**
Institute for Drug Research
School of Pharmacy
Imaging CNS function in health and disease

Dr. **ADI INBAL**
Department of Medical Neurobiology
Institute for Medical Research – Israel-Canada
Hebrew University-Hadassah Medical School
Molecular mechanisms of forebrain and eye development

Former Recipients 2012

Dr. **RONIT SHARON**
Institute for Medical Research Israel-Canada
Hebrew University-Hadassah Medical School

Prof. **RONEN LECKER**
Department of Neurology
Hebrew University-Hadassah Medical School

Dr. **ALEXANDER M. BINSHTOK**
Institute for Medical Research Israel-Canada
Hebrew University-Hadassah Medical School

Prof. **HAIM OVADIA**
Department of Neurology
Hebrew University-Hadassah Medical School

The Hebrew University of Jerusalem
The Authority for Research and Development
https://research.huji.ac.il
Tel: +972-2-658-6625/6/8; Fax: +972-2-561-8196

June 2014

Project coordinator: Ayelet Sagiv
Project editor: Shoshana Glatzer
http://www.facebook.com/JanisDesign

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The Hebrew University of Jerusalem

האוניברסיטה העברית בירושלים
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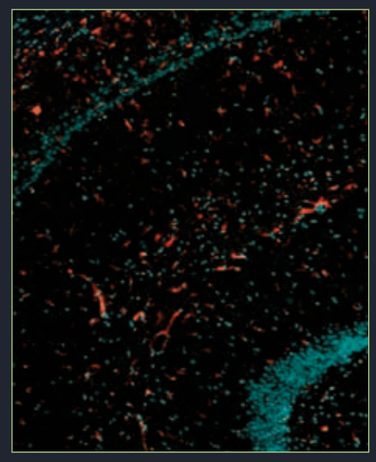
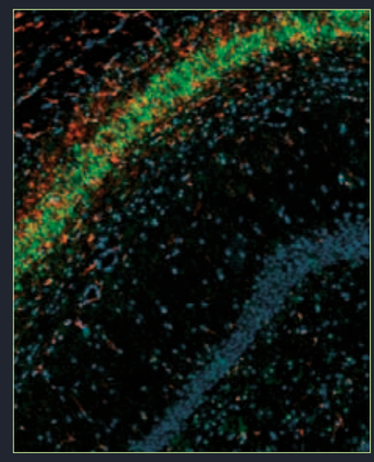
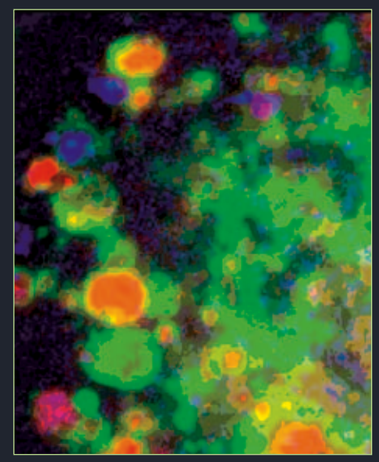
THE PRUSINER-ABRAMSKY RESEARCH AWARDS

תשע"ד 2014

AT THE HEBREW UNIVERSITY OF JERUSALEM

BY THE ORION FOUNDATION

PRUSINER-ABRAMSKY

Research Awards - 2014

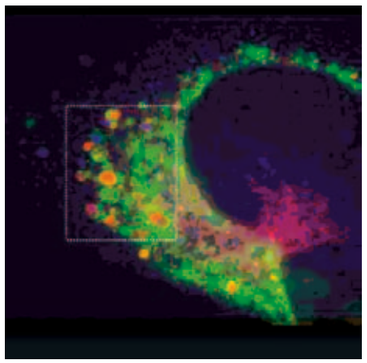
Prof. Stanley B. Prusiner, M.D.

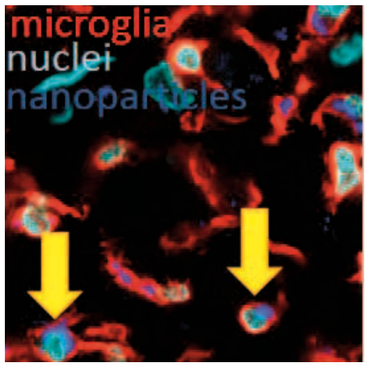
Stanley B. Prusiner, M.D., is Director of the Institute for Neurodegenerative Diseases and Professor of Neurology at the University of California, San Francisco (UCSF), where he has worked since 1972. Born in Des Moines, Iowa, in 1942, he spent his childhood there and in Cincinnati, Ohio. He received his undergraduate degree and medical training at the University of Pennsylvania and his postgraduate clinical training at UCSF. From 1969-72, he served in the U.S. Public Health Service at the National Institutes of Health. He is the author of over 500 research articles and the book *Madness and Memory*.

Prof. Prusiner is a member of the U.S. National Academy of Sciences, the Institute of Medicine, the American Academy of Arts and Sciences, the American Philosophical Society, and a foreign member of the Royal Society of London. He is the recipient of numerous prizes, including the Potamkin Prize for Alzheimer's Disease Research of the American Academy of Neurology (1991); the Richard Lounsbery Award for Extraordinary Scientific Research in Biology and Medicine from the National Academy of Sciences (1993); the Gairdner Foundation International Award (1993); the Albert Lasker Award for Basic Medical Research (1994); the Paul Ehrlich Prize from the Federal Republic of Germany (1995); the Wolf Prize in Medicine from the State of Israel (1996); the Keio International Award for Medical Science (1996); the Louisa Gross Horwitz Prize from Columbia University (1997); the Nobel Prize in Physiology or Medicine (1997); and the U.S. National Medal of Science (2009).

Prof. Prusiner's groundbreaking research on prion diseases, beginning in the late 1970s, led him to propose an explanation for the cause of bovine spongiform encephalopathy ("mad cow" disease) and its human equivalent, Creutzfeldt-Jakob disease, for which he was awarded the Nobel Prize. In this work, he coined the term prion (derived from "proteinaceous" and "infectious") to refer to a previously undescribed form of infection caused by the self-propagation of alternatively folded proteins.

His research has elucidated a fundamental understanding of the proteins underlying such illnesses as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS) and PrP prion diseases. These advances in understanding the molecular, genetic and cellular basis of neurodegenerative diseases have fueled progress toward the development of targeted drug therapies.





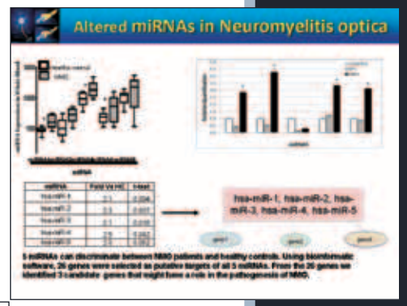
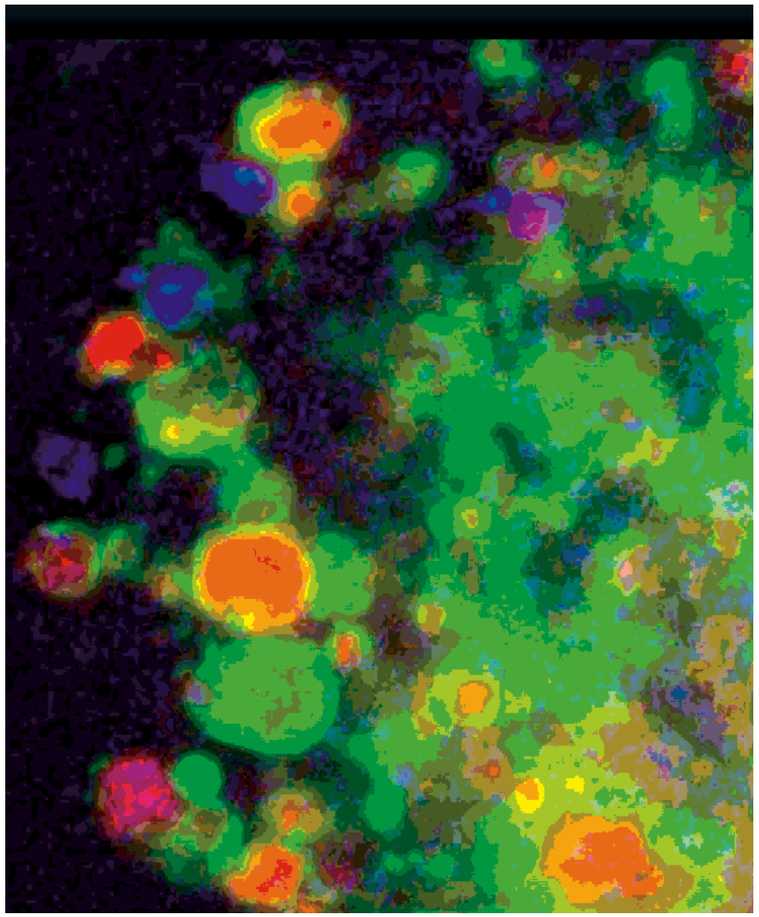
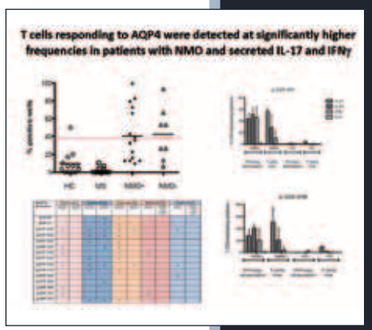


Figure 1. **Patterns of disease progression in epilepsy**

Pattern	pathophysiologic	real
	no. (%)	
Responding 1	48 (28.2)	25 (14.7)
Responding 2	20 (11.8)	19 (11.2)
Relapsing remitting	55 (32.4)	82 (48.2)
Improving	13 (7.6)	10 (5.9)
Progressive	12 (7.1)	13 (7.6)
Stable	22 (12.9)	21 (12.4)

Based on 170 patients from Hadassah's Epilepsy Clinic database, we defined 6 patterns of progression. When seizures induced by stopping treatment were excluded, the pathophysiologic patterns were revealed. Interestingly, women were 2.256 times more likely to belong to the relapsing remitting type of disease progression than men, suggesting an underlying immune pathophysiology in this cases.





PRUSINER-ABRAMSKY

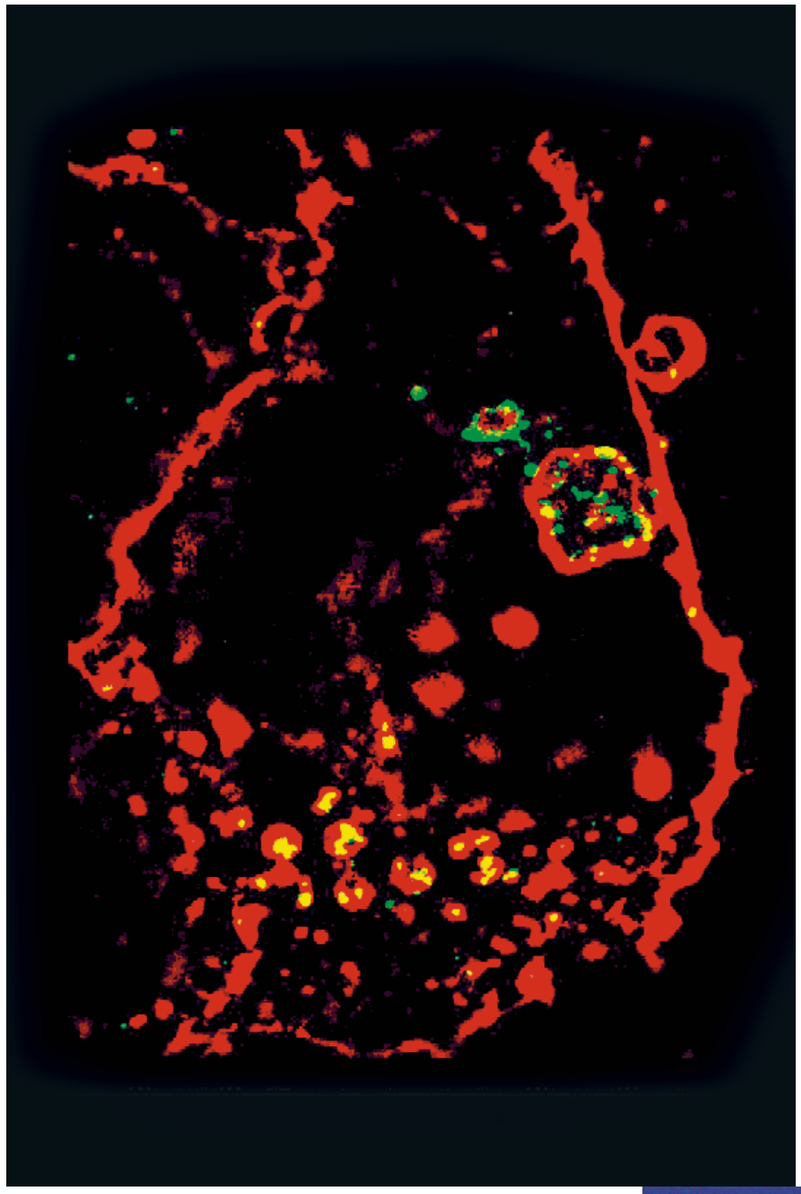
Research Awards - 2014

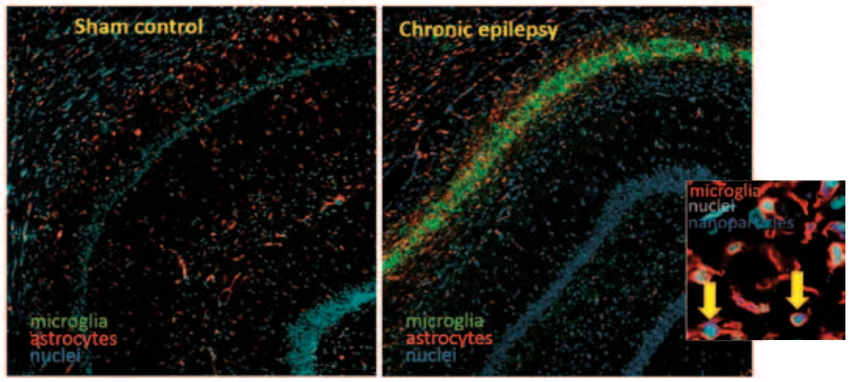
Prof. Oded Abramsky, M.D., Ph.D.

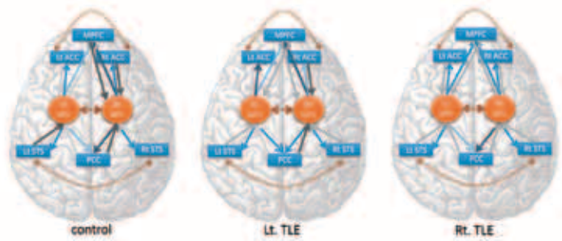
Oded Abramsky was born in Jerusalem and received his M.D. and Ph.D. degrees from The Hebrew University of Jerusalem. He completed his residency in neurology at Hadassah University Hospital, where he was later appointed Head of the Neuroimmunology Unit (1982) and Chairman of the Neurology Department (1988-2005). He was appointed Professor of Neurology at the Hebrew University-Hadassah Medical School in 1982, holding the Israel S. Wechsler Chair in Neurology. He served as Dean of the Faculty of Medicine of the Hebrew University (1992-96) and subsequently was appointed Chairman of the Agnes Ginges Center for Human Neurogenetics at Hadassah University Medical Center.

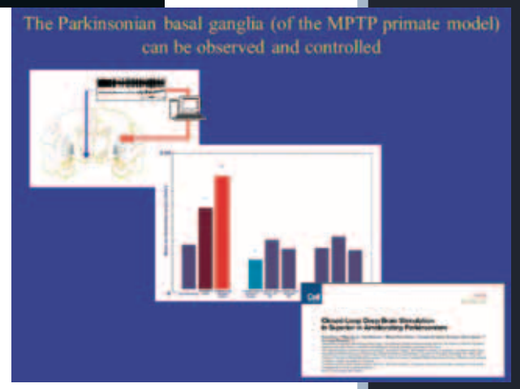
Prof. Abramsky has been actively involved in many aspects of medical research and holds prominent positions in numerous professional organizations concerned with both clinical practice and medical research. He was Chief Scientist of the Israel Ministry of Health (1987-1992), Chairman of the National Medical Research Organization, and served as Chairman of the Israel National Council for Research and Development. He is an Honorary President of the Israel Society of Neuroimmunology; Honorary Member of the American Neurological Association; Member of the Institute of Medicine, National Academy of Sciences (USA); Fellow by Distinction of the Royal College of Physicians (FRCP); and Member of the Israel Academy of Sciences and Humanities, among many other affiliations. In 2008, the Oded Abramsky Chair in Neuroimmunology was established in his honor by Biogen USA at the Hadassah University Medical Center.

Prof. Abramsky's clinical and scientific research focuses on autoimmune neurological diseases. He was a pioneer in the field of neuroimmunology and demonstrated immune pathogenesis in various neurological diseases of the central and peripheral nervous systems and muscle. Indeed, he proved that myasthenia gravis (MG) is an autoimmune disease, and showed the beneficial effect of corticosteroids and chemotherapy on induced experimental MG. His research served as a guideline to successful immunotherapy of MG and many other autoimmune diseases.









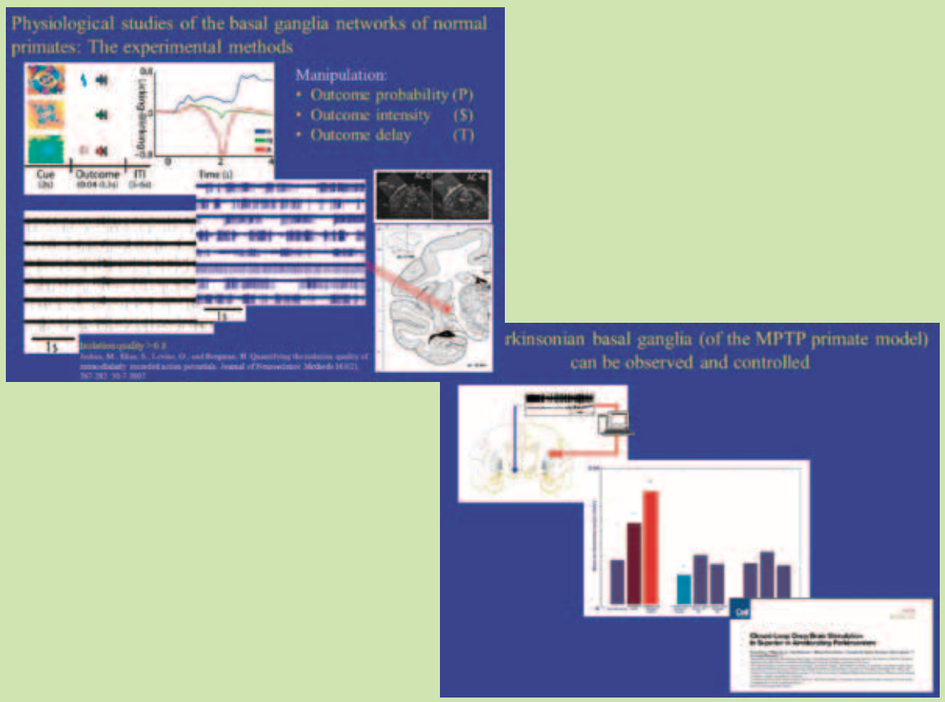
PRUSINER-ABRAMSKY

Research Awards - 2014

The prestigious **Prusiner-Abramsky Research Awards in Clinical and Basic Neuroscience by The Orion Foundation** honor Professors Stanley Prusiner and Oded Abramsky. Prof. Prusiner of the University of California at San Francisco is a Nobel Prize Laureate in Medicine (1997) and an Honorary Doctor of the Hebrew University of Jerusalem.

Prof. Abramsky is the former Chairman of the Neurology Department and a former Dean of the Faculty of Medicine at Hebrew University.

The awards are intended for outstanding researchers from all fields of basic clinical neurosciences at the Hebrew University and the Hadassah University Medical Center.



Prof. **ALBERT TARABOULOS,** Ph.D.
Department of Microbiology and Molecular Genetics
Institute for Medical Research – Israel-Canada
Hebrew University-Hadassah Medical School
Prion Neurotoxicity: From Protein Misfolding to Lipid Disease

Prof. **HAGAI BERGMAN,** M.D., D.Sc.
Department of Medical Neurobiology
Institute for Medical Research – Israel-Canada
Hebrew University-Hadassah Medical School
Computational Physiology and Pathophysiology of the Basal Ganglia and their Disorder – From Understanding to Closed Loop Deep Brain Stimulation Treatments

Dr. **DANA EKSTEIN,** M.D., Ph.D.
Department of Neurology
Hebrew University-Hadassah Medical School
Development of Tools for Patient-Specific Individualized Diagnosis and Treatment of Epilepsy

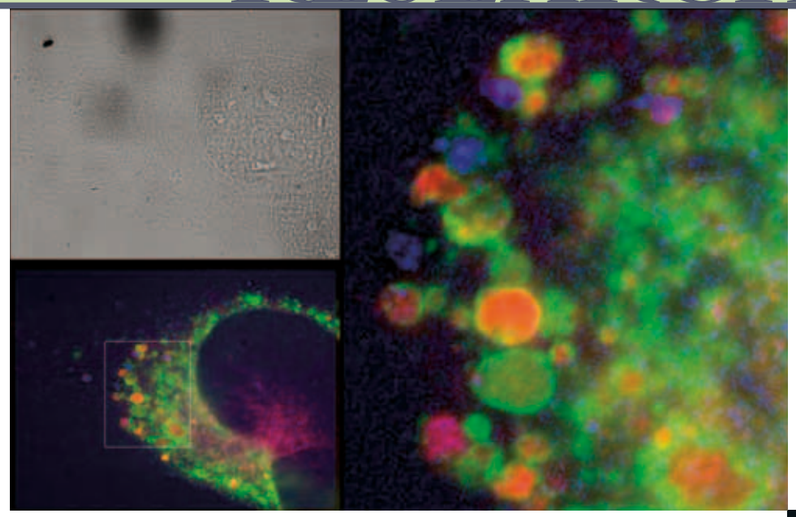
Dr. **ADI VAKNIN-DEMBINSKY,** M.D., Ph.D.
Department of Neurology
Hebrew University-Hadassah Medical School
Personalized Medicine in Multiple Sclerosis and Neuromyelitis Optica: Predicting Disease Outcome and Treatment Responsiveness

RESEARCHERS

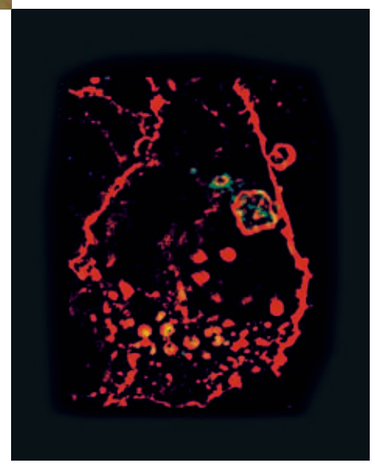
Prof. Albert Taraboulos
Department of Microbiology and Molecular Genetics
Institute for Medical Research – Israel-Canada
Hebrew University-Hadassah Medical School

Albert Taraboulos, the Carolyn Jane Bendheim Professor of Molecular Virology, joined the Hebrew University faculty in 1994, after studying prions with Dr. Stanley Prusiner at UCSF. He has since focused his efforts on these pathogens. He is especially interested in how prions invade and utilize the host cell. He devised ways to visualize prions in cells and tissues, leading to the unexpected discovery of vast prion networks on the surface of cells. He revealed the 'lipid rafts' context of prions, opening new vistas in prion biology and ultimately leading to the realization that prions are toxic to cell membranes.

RESEARCHER



Prion Neurotoxicity: From Protein Misfolding to Lipid Disease



Prions cause fatal neurodegenerations such as Creutzfeldt-Jakob disease. Prion diseases can be infectious, familial or spontaneous. Surprisingly, little is known about how these pathogens destroy brain cells. Prof. Taraboulos and his team have now discovered that prions cause abnormalities in cholesterol and associated lipids in infected cells.

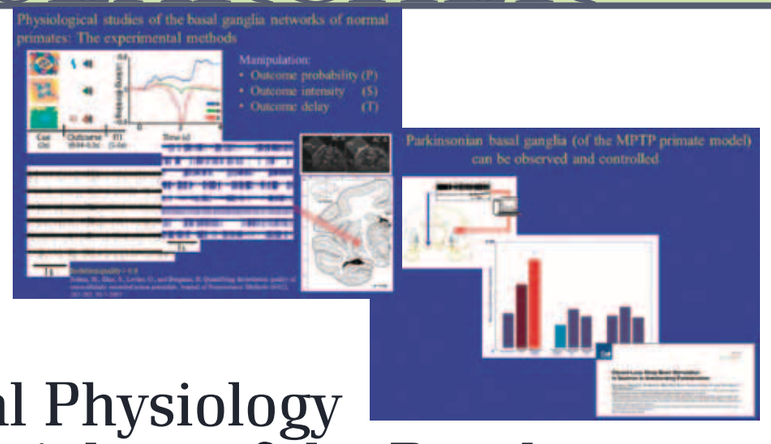
Prions infect patients by hijacking one of their own proteins, turning it into a malignant conformation prone to aggregate. Having recently discovered amyloidic prion networks on the surface of cells, they propose that it is the *aggregation of prions on cellular membranes that ignites neurotoxicity.*

Their data suggest that aggregates of prions interact with membranes to induce the coalescence of 'cholesterol rafts,' perturb cholesterol transport, and engender widespread anomalies in infected cells. If validated, this would be a revolutionary mechanism by which *misfolded proteins generate a lipid disorder*. This novel avenue in prion pathology will be explored to determine whether similar mechanisms also play a role in other neurodegenerative diseases, such as Alzheimer's disease.

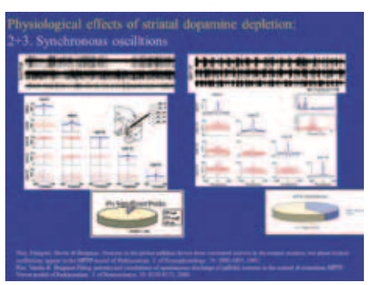
Prof. Hagai Bergman
Department of Medical Neurobiology
Institute for Medical Research - Israel-Canada
Hebrew University-Hadassah Medical School

Hagai Bergman, the Simone and Bernard Guttman Chair in Brain Research, earned his M.D. and D.Sc. from the Technion in 1984. His post-doctorate fellowships were at the Hebrew University of Jerusalem and Johns Hopkins Medical School, Baltimore. In 1990, he started his own research group at the Hebrew University and was appointed full professor in 2004. He was one of the founding members of the Interdisciplinary Center for Computational Neuroscience (ICNC) and of the Edmond and Lily Safra Center for Brain Research (ELSC) and remains active in both. As part of the Hadassah Hospital deep brain stimulation (DBS) group since 2003, he has performed electrophysiological mapping in ~ 400 procedures.

RESEARCHER



Computational Physiology and Pathophysiology of the Basal Ganglia and their Disorder – From Understanding to Closed Loop Deep Brain Stimulation Treatments



Prof. Bergman's previous studies revealed the emergence of synchronous oscillations in the cortex and basal ganglia of MPTP*-treated Parkinsonian monkeys and human patients with advanced Parkinson's disease undergoing deep brain stimulation (DBS) procedures. Recently, he showed that closed loop deep brain stimulation is superior to standard open-loop stimulation in the MPTP primate model of Parkinson's disease. His current research program is aimed at finding the optimal closed loop strategies in human patients with Parkinson's disease, as well as in the ketamine/PCP (NMDA antagonist) primate model of schizophrenia. If successful, his lab's research will pave the way for improved therapy for human patients with severe brain disorders, including Parkinson patients and schizophrenia.

* 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, a neurotoxin which causes permanent symptoms of Parkinson's disease by destroying brain dopaminergic neurons

Dr. Dana Ekstein
Department of Neurology
Hebrew University-Hadassah Medical School

Dana Ekstein is a graduate of the Hebrew University-Hadassah Medical School, receiving her M.D. in 1997, and her Ph.D. (in the Department of Medical Neurobiology) in 2013. During her residency, Dr. Ekstein became interested in epilepsy and did her doctoral studies on the electrophysiology of epileptogenesis in Prof. Yoel Yaari's laboratory. Having trained in the clinical management of epilepsy, she joined and initiated research projects on the study of herbal therapies for epilepsy and on the use of direct current stimulation for treatment of status epilepticus in rats. Since 2010, Dr. Ekstein is a senior neurologist in the Department of Neurology and serves as acting director of the Comprehensive Epilepsy Center at Hadassah.

RESEARCHER

Development of Tools for Patient-Specific Individualized Diagnosis and Treatment of Epilepsy

Figure 1. **Patterns of disease progression in epilepsy**

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Responding 1	48 (28.2)	25 (14.7)
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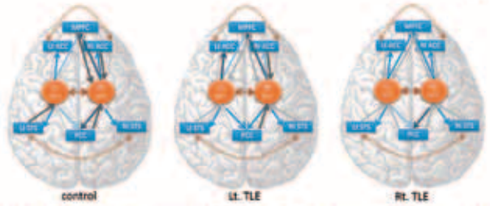
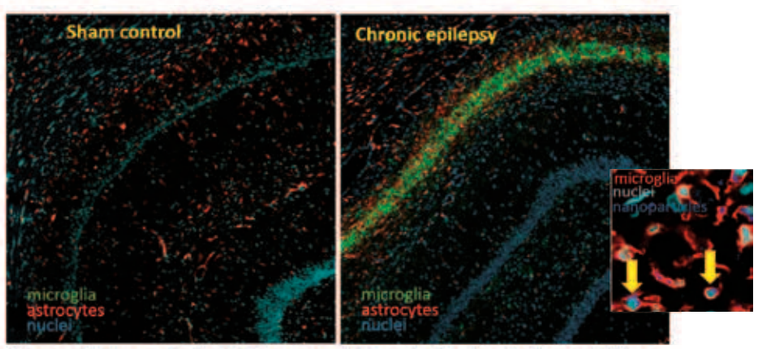
Figure 2. **EEG effective connectivity in patients with temporal lobe epilepsy**



We analyzed resting state normal appearing EEGs of 16 patients with temporal lobe epilepsy (TLE) and 4 controls, using Dynamic Causal Modeling in SPM12. We found that more healthy subjects have stronger right than left connections, in comparison to subjects with TLE and especially right TLE. More subjects with left TLE have stronger left than right connections, in comparison to healthy controls.

Figure 3. **Molecular imaging of inflammation in epilepsy**



Nanoparticles were injected intravenously to rats with chronic temporal lobe epilepsy (induced by pilocarpine status epilepticus) and to control rats. Astrocytic and microglial activity was seen in the brains of chronically epileptic rats, especially in the CA1 area. Six hours following the injection, fluorescent nanoparticles were detected inside microglial cells in the hippocampus (inset).

The ultimate goal of this research is to build tools that will help in the individualized diagnosis of people with epilepsy and enable tailoring of patient-specific treatments. Dr. Dana Ekstein proposes a novel classification of epilepsies based on their pattern of disease progression, which will enable additional pathophysiologic-based stratification of the patients' population. Computational analysis of normally appearing EEG effective connectivity in people with epilepsy may be used as a tool for correct diagnosis and for sub-classification of patients, based on their brain network activation. Nanoparticles are used to develop molecular imaging able to detect and demarcate inflammation in a rat model of chronic epilepsy. These diagnostic tools may be directly applied to guide standard and experimental pharmacological and non-pharmacological treatments, and also to shape future research on the pathophysiology of epilepsy.

Dr. Adi Vaknin-Dembinsky
Department of Neurology
Hebrew University-Hadassah Medical School

Born in Rehovot, Dr. Vaknin-Dembinsky received both her M.D. and Ph.D. (in Biochemistry) at the Hebrew University of Jerusalem. After her residency in Neurology at Hadassah University Hospital, she was awarded a Multiple Sclerosis Fellowship at Brigham & Women's Hospital, at Harvard University, before returning to the Department of Neurology. She is currently a Senior Lecturer in Neurology at the Hebrew University-Hadassah Medical School. Dr. Vaknin-Dembinsky is a member of the Executive Board of the Israel Society of Neuroimmunology and has co-authored dozens of scientific publications.

RESEARCHER

Personalized Medicine in Multiple Sclerosis and Neuromyelitis Optica: Predicting Disease Outcome and Treatment Responsiveness

The focus of Dr. Vaknin-Dembrinsky's scientific work is the immune responses involved in CNS demyelinating diseases - multiple sclerosis (MS) and neuromyelitis optica (NMO). Her research group has established a large patient database, which includes computerized clinical, imaging and peripheral blood mononuclear cell banks from MS and NMO patients. Using molecular and cellular techniques, they study the ability of a set of genes to predict disease outcome and response to MS therapy. Additionally, they study specific markers that will improve NMO diagnostic and promote our understanding of the disease etiology.