



# Drug Discovery, Design and Delivery Research

**The Science of Good Medicine**

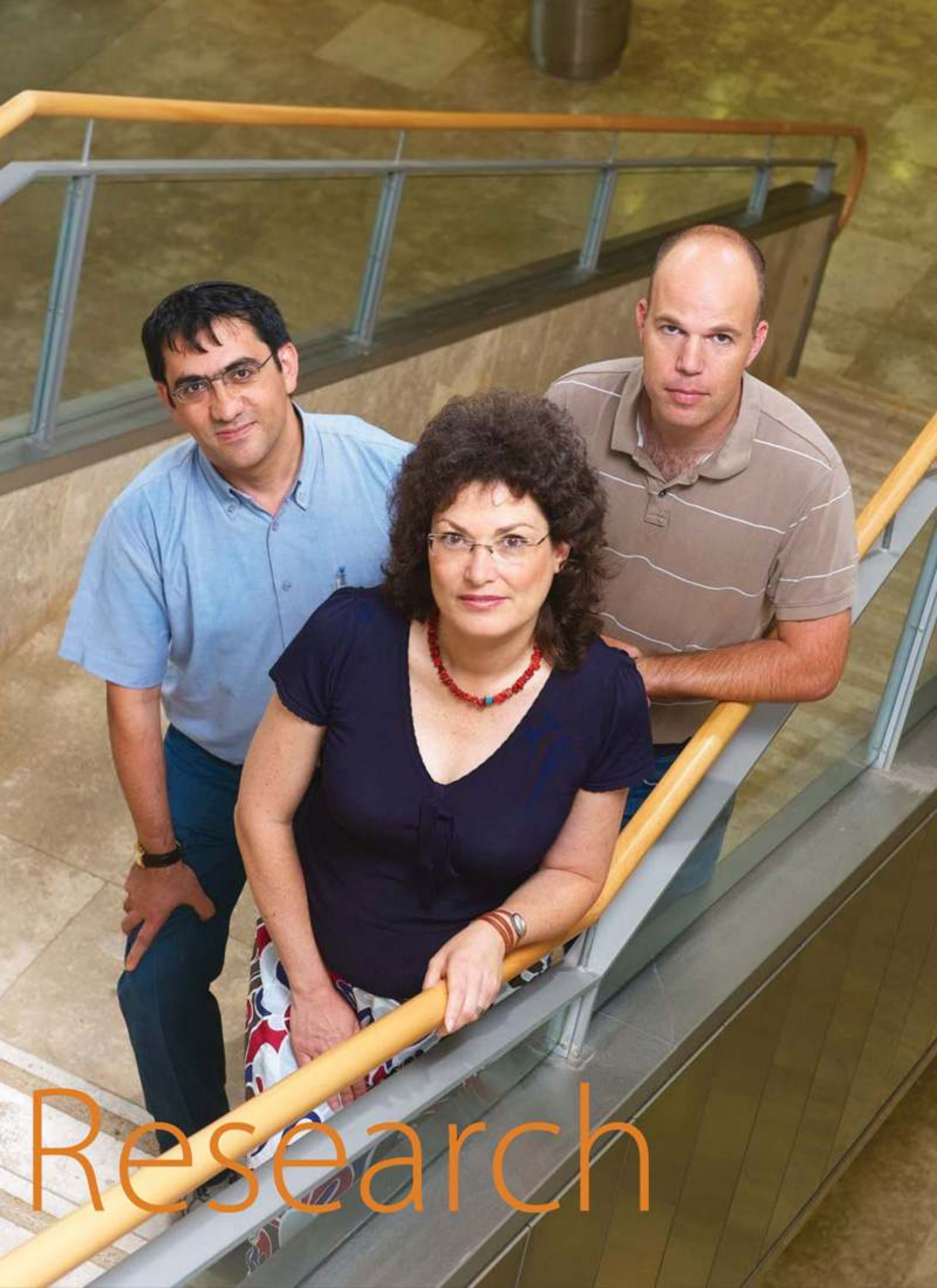


Bar-Ilan University

→ → → By examining wellness and disease from the molecular to the clinical to the societal level, Bar-Ilan University is writing a prescription for a healthier future.

Pictured from left to right: →  
Dr. Shai Rahimipour  
Prof. Bilha Fischer  
Dr. Ehud Banin

# Druid Delivery



Research



Louis Pasteur

**When** it comes to discovering the drugs that save lives, chance favors the prepared mind.

This statement – attributed to Dr. Louis Pasteur – aptly describes the convergence of scientific disciplines that are powering medically significant discoveries at Bar-Ilan University.

In laboratories all over the campus, Bar-Ilan researchers are “preparing minds” by identifying molecular factors that trigger illness; by modeling, synthesizing and testing new compounds for intervention; and by designing path-breaking strategies for effective drug delivery. At the same time, they are creating techniques needed to confront tomorrow’s medical challenges.

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## Where It All Began

The work of Prof. (Emeritus) Abraham Nudelman illustrates how cross-disciplinary investigation can bring new medicines to light. The founding Director of BIU’s Medicinal Chemistry Division, within the Department of Chemistry, Nudelman began his career in cancer research. But when he stumbled upon an article proving that patients who take medication for diseases of the central nervous system have a lower-than-average incidence of brain cancer, he and a colleague at Beilinson Hospital had an idea. They created hybrid molecules in which a common schizophrenia medication served as a “delivery vehicle” for transporting anti-cancer drugs into the brain.

Nudelman’s research soon led to another discovery: a highly effective drug for schizophrenia. With Phase II clinical trials completed, Nudelman’s compound is poised to become one of only a handful of Israeli-developed drugs to reach the market. Based on research taking place in Bar-Ilan laboratories, however, more life-saving discoveries will not be far behind.

➔ **BIU scientists are isolating factors that contribute to cancer formation.**

## Combating Cancer

BIU scientists in the Nina and Everard Goodman Faculty of Life Sciences are isolating factors that contribute to cancer formation, and identifying targets for drug-based intervention. Prof. Uri Nir, Dean of the Faculty, has revealed a “smoking gun” – an enzyme that, in several tissue types, plays a pivotal role in cancer onset. Prof. Ronit Sarid’s work focuses on a “sleeper” virus that quietly infects the body for years before triggering Kaposi’s sarcoma – a type of tumor most commonly associated with AIDS. Dr. Shulamit Michaeli is designing RNA-protein complexes that can shut down cancer-causing genes before they start. And Dr. Sol Efroni is quantifying the network-wide changes that occur when normal tissue becomes malignant.



Other BIU scientists are examining how cancer spreads. Dr. Mira Barda-Saad has demonstrated how filaments that normally appear on a cell's surface – the same filaments that allow cells to latch on to each other and travel between tissues – have a substantially different shape in the presence of cancer. By identifying a specific protein that causes this structural abnormality, she has defined an important new target for anti-cancer drugs.

## Nervous System News

In work that is revealing new strategies for rational drug design, BIU biophysicist Dr. Yoav Paas is examining how electrochemical signals are transmitted in the brain, and how this process is altered in conditions ranging from epilepsy, to irritable bowel syndrome, to the craving for nicotine. In another lab, Prof. Gal Yadid has demonstrated how medication can moderate the brain activity associated with cocaine-seeking behavior – a discovery that may lead to the development of drugs that combat addiction.

In BIU research on neurodegenerative disease, Prof. Bilha Fischer has identified protective agents that may minimize the effects of Alzheimer's disease. Dr. Shai Rahimipour has created molecules that inhibit the build-up of plaques – excess amyloid beta protein that, in Alzheimer's patients, causes brain cells to die. He has also identified molecular agents that protect nerve cells from multiple sclerosis symptoms. And Prof. Amnon Albeck has demonstrated how a rare metal may help restore normal neural function in Parkinson's patients.

➔ **BIU researchers are revealing new strategies for rational drug design.**

Moving from the brain to the peripheral nervous system – those cells, found in the fingers and limbs that contribute to movement and sensation – Prof. Ron Goldstein is defining targets for drug development by



examining genes that affect human nerve regeneration after damage. Since damage to the peripheral nervous system is the most common neurological syndrome associated with AIDS treatment, Prof. Goldstein's work may have significant impact on the development of new drugs for AIDS patients.

## Targeting Diabetes and Glaucoma

Many diseases can be traced to abnormalities in our DNA. Prof. Bilha Fischer has turned this idea on its head by pioneering the use of nucleotides – the tiny building blocks from which DNA is constructed – as the active ingredient in disease-fighting compounds. In her laboratory, she has introduced changes into nucleotides that make them more stable, and allow them to bind to specific targets – both qualities vital for effective drug interaction. Her research has identified promising drug candidates for both Type II (adult onset) diabetes and glaucoma.

## Immunity and Infection

Prof. Benjamin Sredni has shown how special molecules help the immune system “shift gears” so that it can more effectively combat cancer and infection. Prof. Sredni's work is also clarifying the immune system's role in a number of other conditions, including Alzheimer's, lupus and diabetes. In another project, Profs. Aharon Gedanken and Ronit Sarid have synthesized nanoparticles that block certain viral infections.

One of the most difficult problems in drug development is antibiotic resistance. Dr. Ehud Banin has shown how bacteria under attack by the body's immune system team up to form antibiotic-resistant

biofilms that serve as “safe havens” for disease-causing pathogens. By clarifying this mechanism, Dr. Banin is contributing to the fight against antibiotic resistance, as well as the search for new treatments for biofilm-related diseases such as cystic fibrosis.

## Faster Drug Discovery

Because of recent advances in robotics and miniaturization, biomedical researchers can screen huge numbers of molecules, panning for the “gold” that will be of significant therapeutic value. Prof. Gerardo Byk is fueling these advances by developing automated synthesizing and screening techniques. Computer-aided drug design is also being advanced, with Prof. Byk, Prof. Michael Shokhen and Dr. Hanoach Senderowitz all pursuing research designed to quickly “zero in” on medically promising compounds. Such computational methods have greatly accelerated drug design efforts in the fight against AIDS, and could help provide a rapid response to other threats, including influenza, bio-terrorism and chemical warfare.



## Drug Design and Testing

A well-designed drug works like a key – locking onto the surface of a disease-causing molecule, it blocks its activity and renders it harmless. But to design a good key, you need a very accurate picture of the lock. Dr. Yitzhak Mastai has created a new technique that

allows scientists to distinguish between chiral pairs – pharmaceutically significant molecules that may look alike, but are actually mirror images of one another. Another BIU researcher working on the imaging of molecular interactions is Prof. Aryeh Weiss, who uses a fluorescent microscopy technique to track dynamic processes important to understanding how a drug will work in a living system. Nuclear magnetic resonance (NMR) studies performed by Dr. Jordan Chill round out the picture, by providing three-dimensional images of medically-important proteins situated near the cellular membrane.

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Once a drug candidate is identified, it must be tested. Prof. Ron Goldstein has developed a low-cost platform that uses chick eggs to test drugs employed in the treatment of blood cancers such as leukemia and myeloma, as well as allergy testing.

More efficient clinical trials in humans are also in the pipeline, thanks to the work of Prof. Jonathan Rabinowitz, of the Louis and Gabi Weisfeld School of Social Work. Prof. Rabinowitz heads an EU working group that is developing advanced data analysis techniques for evaluating anti-psychotic and anti-depressant medications.



## Targeting Tissues

Prof. Shlomo Margel has produced injectable nanoparticles that can target specific cells, releasing cancer-fighting drugs directly into tumors. Prof. Benjamin Ehrenberg also uses nanoparticles as a vehicle for delivering anti-cancer drugs, but activates those drugs with light – creating a highly focused, “smear-on” protocol for the treatment of tumors near or on the skin surface. Prof. Aryeh Frimer is improving light-activated chemotherapy by fine-tuning the positioning of nanoparticles within the cellular membrane. Prof. Aharon Gedanken uses sono-chemistry – the manipulation of materials with microwave radiation – to produce micro-vehicles that deliver fast-release antibiotics and anti-cancer drugs. Finally, Prof. Gerardo Byk is developing a method for delivering genes directly to cancerous tissues – genes that, when activated, would trigger cell death.

## Toward a Healthier Future

*The human genome project has given scientists an entirely new toolbox, filled to the brim with unexplored possibilities for manipulating the molecular factors that control both health and disease. The convergence of this biology-based windfall with dramatic advances in both information technology and nanoscience is making Bar-Ilan University one of the most exciting places in the world for pursuing drug discovery research.*

*Bar-Ilan was the first Israeli university to launch a dedicated program in Medicinal Chemistry. By continuing to invest in research supporting drug design, discovery and delivery, Bar-Ilan is proving its continued dedication to saving lives all over the world.*



For more about the research of BIU faculty listed in this brochure go to: [www.biu.ac.il](http://www.biu.ac.il) and click Research.



BIU's Leslie and Susan  
Gonda (Goldschmied)  
Nanotechnology Triplex

## Bar-Ilan University Science and Technology

Bar-Ilan University stands at the forefront of cutting-edge research. Bar-Ilan researchers are making breakthroughs that improve life around the globe in areas such as drug-development, nanotechnology, medical research, bio-engineering, microscopy, optics, communications, energy, security, and more. As part of a national program to combat Israel's brain drain, BIU has taken the lead by committing to absorb dozens of returning experimental scientists within its world-class research infrastructure, and has added state-of-the-art physical facilities in engineering, brain sciences and nanotechnology to house these innovative initiatives. The Science and Technology Series highlights some of the University's most exciting research endeavors.



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