



# Cancer Research

**Where the Cure Begins**



Bar-Ilan University

→ → → At Bar-Ilan University, a multi-disciplinary approach to research is making inroads in the global war against cancer. Looking beyond just the destruction or surgical removal of tumors, Bar-Ilan researchers are exploring the body's ability to heal itself, while creating new protocols for targeted treatment.

Pictured from left to right: →  
Prof. Ramit Mehr  
Prof. Ronit Sarid  
Dr. Cyrille Cohen  
Dr. Shay Ben-Aroya  
Dr. Mira Barda-Saad

Where  
the Cure



Begins



Rudolf Virchow

**A century** and a half since German doctor and anthropologist Rudolf Virchow – often referred to as the “father of modern pathology” – used a microscope to characterize the difference between normal and malignant cells, cancer still causes millions of deaths every year. Even for those who beat the disease, clinical treatment can be harrowing. Radiation and chemotherapy can cause hair loss, nausea and debilitating weakness. Worse, they can devastate the immune system, leaving the patient exposed to infection and even death.

At Bar-Ilan University, a multidisciplinary approach to research is making inroads in the global war against cancer. Looking beyond just the destruction or surgical removal of tumors, Bar-Ilan researchers are exploring the body’s ability to heal itself, while creating new protocols for targeted treatment.

One of the world’s foremost centers for cancer immunology, Bar-Ilan is home to scientists who are developing strategies for enhancing the body’s natural ability to block tumor formation. Bar-Ilan laboratories are also breaking new ground in the areas of cancer genetics and genomics, tumor dynamics, targeted drug treatment and advanced medical imaging.

By creating partnerships between bio-based scientists and colleagues trained in nanotechnology, computer science, chemistry and physics, Bar-Ilan is helping to crack the mystery of cancer, while leading the charge toward improved prevention, diagnostics and treatment.

## De-Mystifying Cancer Mechanisms

Can the human body be induced to protect itself from cancer, and overcome tumor formation once it starts? This is the question being asked by Dr. Mira Barda-Saad and her colleagues. An expert in molecular immunology, Barda-Saad is currently examining the activation of “natural killer” lymphocytes – fast-acting cells of the innate immune system that serve as the body’s first line of defense against both viruses and cancerous tumors. By clarifying how natural killer cells distinguish between normal body tissues and cancer, Barda-Saad hopes to identify new targets for drugs that would activate – and amplify – the immune system’s cancer-fighting potential.

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In another lab, Dr. Jeremy Don studies molecular factors involved in cancer onset. Ten years ago, Don identified a gene implicated in human lymphoma. More recently, he demonstrated how, under certain circumstances, this lymphoma-related gene can inhibit the growth of other types of malignancies. Don also identified and cloned a gene vital to maintaining DNA’s structural integrity. DNA fragmentation is a hallmark of cancer, and Don’s work may point toward a new approach to preventing fragmentation, thus “short-circuiting” cancer on the genetic level.

Prof. Doron Ginsberg’s research focuses on a family of genetic factors that play a critical role in cell proliferation and the cessation of cell growth – processes that are abnormal in the presence of cancer. Ginsberg’s recent work indicates that one member of



this family of factors is involved in autophagy – a normal process in which a cell destroys proteins and other substances situated inside the cellular membrane. Autophagy may protect cancer cells by destroying anticancer drugs, and Ginsberg is examining this possibility by studying the way this genetic factor interacts with chemotherapeutic treatments.

In the laboratory of Dr. Yaron Shav-Tal, new imaging techniques based on time-lapse fluorescent microscopy are making it possible to characterize genetic processes that occur inside the living nucleus. While focusing mainly on how genes are switched “on” and “off” in normal cells, he is also looking at how this process differs in the case of cancer.

Moving from genetic factors to enzymes, Prof. Uri Nir has revealed a “smoking gun” – a specific enzyme that plays a pivotal role in the onset of colon, prostate and breast cancers. The fact that this same enzyme-based mechanism appears in all these cancers indicates that Nir may have found an important molecular junction where normal tissues turn cancerous. Currently Prof. Nir is engaged in developing new anti-cancer drugs that will target this key regulatory enzyme.

→ **BIU’s culture of multi-disciplinary collaboration reflects a “systems approach” that is bringing the complex pathology of cancer into clear focus.**

### Systems Biology and Cancer

While some BIU researchers are seeking out individual molecular factors that lead to cancer, others are examining system-wide patterns that characterize various cancer types, as well as individual cancer patients.

When a body cell replicates itself, a copy of its genome – the sum total of its genetic material – is passed down to the next generation. But in the case of cancer, cell replication is unstable. Using yeast as a model, Dr. Shay

Ben-Aroya is mapping out the complex interactions that ensure genome maintenance and stable chromosome transmission in both yeast and in human body cells. This will allow him to identify specific genes that promote a predisposition for cancer, as well as molecular targets for novel anti-cancer therapies.

Dr. Yanay Ofran also takes a systems-based approach to cancer – or more specifically, to cancer patients. Seeking to understand why patients with identical diagnoses often respond differently to treatment, Ofran is examining tiny genetic variations referred to as Single Nucleotide Polymorphisms, or SNPs. Ofran is looking at how SNPs – which usually do not produce physical changes – may predispose people to disease and influence their response to drugs. He is also examining how certain SNP combinations are linked to specific tumors and treatment outcomes. Ofran is also using genomic data to predict how patients will respond to various combinations of chemotherapeutic medications.

Finally, Prof. Avidan Neumann is using computerized tools to simulate the body's response to pathogens, and track the progress of disease. An expert on the evolution of infectious agents including HIV, Neumann is now starting to apply his modeling techniques to cancer antigen dynamics.

## Using Immunity

Traditional anti-cancer treatments are often more painful than the disease itself. That's why a number of Bar-Ilan researchers are developing strategies that involve activating the immune system to defend the body against cancer.

Working with Prof. Michael Albeck, noted immunologist Prof. Benjamin Sredni has synthesized a compound that significantly stimulates immune function. Called AS101, this non-toxic compound – now in Phase II Clinical Trials – has been found to prevent the drastic drop in white blood cell and platelet production

that is sometimes induced by chemotherapy. More importantly, AS101 is able to turn tumors that were impervious to chemotherapy into tumors that respond to chemotherapeutic treatment.

White blood cells generated within malignant tissues can serve as potent anti-cancer agents. However, such cells are notoriously difficult to isolate. Recently, Dr. Cyrille Cohen and his colleagues have overcome this hurdle by devising a gene-therapy-based method for transforming normal, "naive" white blood cells into tumor killers. Cohen is currently working on improving his technique, by generating immune cells that sustain themselves over a longer period of time in the body, and have the ability to target specific malignancies such as lung, liver or breast cancer.

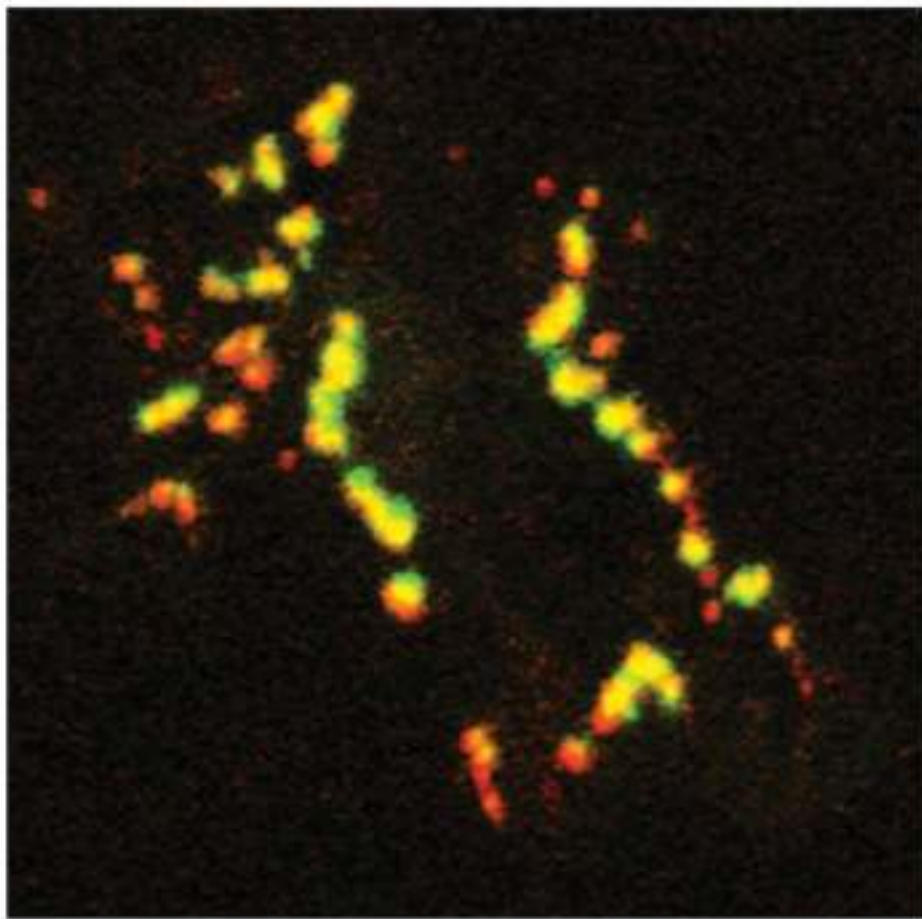
→ Our researchers are examining system-wide patterns that characterize various cancer types, as well as individual cancer patients.

Fighting cancer requires a strategy, and strategy is the specialty of Prof. Ramit Mehr, a computational immunologist who uses mathematical models, computer simulations and bioinformatical techniques to understand immune system dynamics. Mehr has created models for how the immune system will behave in the presence of cancer and other diseases. In a recent project, Mehr devised a novel method for analyzing the genetic mutations in lymphomas, which are cancers of antibody-forming cells. Her work has demonstrated that the molecular factors triggering cell death or promoting survival in lymphoma cells – as well as those cells involved in the chronic inflammation that can lead to cancer – are different from the factors that determine cell death and survival in normal, non-cancer-related cells.

# Where the Cure Begins

## Drug Discovery and Delivery

Exciting research focusing on new drug-based methods for fighting cancer is taking place in the lab of Prof. Shulamit Michaeli. An expert on "silencing" RNA – genetic material that prevents the expression of specific genes – Michaeli designs and synthesizes RNA-protein complexes that inhibit the function of a variety of genes that trigger cancer. The silencing RNA is delivered by a nanosized inorganic particle created in collaboration with Prof. Jean-Paul Lellouche.



Prof. Uri Nir also uses nanosized vehicles to deliver cancer-fighting drugs directly to malignant cells. Working together with Dr. Yoav Paas, Nir's techniques may make it possible to achieve better results with lower doses, leading to a reduction in chemotherapy-related side effects.

Another scientist whose work may improve chemotherapy is Dr. Rachela Popovtzer. Popovtzer synthesizes gold nanoparticles that – when

administered to a patient by IV drip – target and attach to malignant cells. This, in turn, creates a "golden" signal on a CT scan that reveals the exact location of cancer within the body, providing a clear target for targeted chemotherapy, as well as an important "early warning" system for cancer metastasis. In another project, Popovtzer has created gold nanorods that heat up when exposed to near-infrared light. These nanorods – which attach themselves to cancer cells – can be activated non-invasively by light from the skin surface, destroying the cancer while leaving non-cancerous tissue unharmed.

In another nanotechnology-based project, Prof. Ronit Sarid is collaborating with Prof. Aharon Gedanken on a system that prevents herpesviruses – pathogens that, in a minority of cases, can trigger a cancer known as Kaposi's sarcoma – from docking at the cellular membrane. This basic science may eventually be applied to preventative treatments for Kaposi's sarcoma.

Finally, it may soon be easier to develop effective anti-cancer drugs, thanks to a rapid and economical system for developing and screening chemotherapies developed by Prof. Ron Goldstein. Focusing on leukemia and other blood cancers, Goldstein and his colleagues use bird embryos – a model that has been used for decades in research on human cancer – as a platform for testing how blood cancers react to various chemotherapy agents.

### *Cancer is a Disease. Not a Sentence.*

*At Bar-Ilan University, researchers are closing in on cancer's causes, while pioneering new approaches to prevention and treatment. BIU's culture of multi-disciplinary collaboration reflects a "systems approach" that is bringing the complex pathology of cancer into clear focus, and giving all of us greater hope for a healthy future.*



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.

# research



BIU's Lilly Shapell  
Central Promenade

## 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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