Bar-Ilan University
The Azrieli
Faculty of Medicine

אוניברסיטת בר-אילן
הפקולטה לרפואה
ע"ש עזריאלי

The Azrieli Faculty of Medicine in the Galilee
Bar-Ilan University

The Azrieli Faculty of Medicine of Bar-Ilan University was established in 2011 in the heart of the upper Galilee, in Safed, and is the pride and joy of BIU. It **aspires to generate a transformative change in health that will lead the Galilee to become the Health Capital of Israel, in effect positively impacting on the entire country.**

The Faculty ascribes great importance to the study of health and disease unique to the Galilee population with the objective of improving health services for the residents of northern Israel, meeting their needs and ultimately benefiting all of the people of Israel. Faculty researchers are making innovative breakthroughs in healthcare research that will benefit humanity by helping prevent and cure chronic disabling and life-threatening disease. It is also involved in science enrichment programs for the Galilee high school students, preventive medicine, promotion of health and wellness, and in environmental health.

Since its opening, 23 principal researchers have joined the Faculty of Medicine (http://research.md.biu.ac.il/labs/). Nearly all of the researchers at the Faculty of Medicine were recruited from internationally recognized institutions within the framework of the Returning Scientist initiative, and have been rapidly and cohesively integrated into Israel's robust biomedical and health research community through the Faculty.

The Azrieli Faculty offers the following MD programs:

- The three-year program - for students who have successfully completed three years of pre-clinical medical studies at a recognized medical school abroad.
- The four-year program – for students who have successfully completed their undergraduate degree studies, with a background in scientific disciplines.

The faculty also offers:

- Graduate studies in biomedical and population health disciplines - M.Sc. and Ph.D. programs with 150 enrolled graduate students.
- The Faculty "Galilee Stars" program - designated to attract residents to medical centers in the Galilee, by offering educational enrichment and research fellowships as part of the medical specialty residency.

Contemporary medicine progresses through advances in research and innovative initiatives. To this end, the Faculty has established advanced research centers at both the Faculty campus and the affiliated hospitals. Research topics cover a wide spectrum of biomedical questions, from

the basic level of proteins and the cell, through the biological systems of the body, to the wide area of population health.

Emphasis is placed on several research topic areas. Translational research (research that is specifically designed to improve health outcomes) is key at the Faculty:

- Population health with an emphasis on equality in health and wellbeing
- Diabetes and metabolic diseases
- Genomic medicine
- Microbiome and Immunity
- Convergence of Artificial and Human Intelligence in the Service of Health
- Research and Innovation in medical education
- Medical humanities and bioethics

We are affiliated with the following Israeli medical centers:

- Padeh (Poriya) Medical Center, Tiberias
- Ziv Medical Center (Rebecca Sieff Hospital), Safed
- Galilee Medical Center, Nahariya
- Nazareth Hospital EMMS (Scottish Hospital), Nazareth
- The Holy Family Hospital, Nazareth (Italian hospital)
- Mazra Hospital, Acre

BIU International - List of research groups from the Azrieli Faculty of Medicine

Cancer

PI's name	Research scope + link to group's website	Brief research description
Dr. Michael Blank	Molecular and Cellular Cancer Biology	The laboratory investigates the molecular processes operating in and leading to generation of cancer cells (the process is known as a carcinogenesis), cancer progression, as well as mechanisms underlying the ability of tumor cells "to escape" the destructive impact of anticancer therapies used in clinics. In particular, we study the role that Smurf2, a HECT type E3 ubiquitin ligase and recently identified tumor suppressor

		(Blank et al. Nature Med 2012; Zou et al. BBA-Rev Cancer 2015; Emanuelli et al. Cancer Res 2017), plays in the ability of cancer cells to replicate, metastasize and hinder the effects of anticancer therapies. The research program addresses key questions in cancer biology: What are the fundamental molecular mechanisms operating in cancer? How are they regulated? How do they affect tumor cell sensitivity to anticancer therapies? And, most importantly, how can we target cancer-related molecular networks to cure this devastating disease.
Dr. Milana Frenkel-Morgenstern	Cancer Genomics and BioComputing of complex diseases	The research in the cancer genomics and BioComputing lab focuses on the following topics: Liquid biopsy of low burden tumors using circulating cell-free DNA; Chimeric Protein-Protein Interactions (ChiPPI) analysis and their role in altering cancer-specific phenotypes; Pan-Cancer data analysis to study the similarities and differences across diverse tumor types; Liquid Biopsy using cell free DNA in Glioblastoma. Comparative genomics and protein domain evolution; Codon-usage analysis and cell-cycle regulation; Analysis of miRNA sequences for evolutionary differences.
Dr. Meital Gal-Tanamy	Molecular Virology	Our Lab leads a research that will contribute to the rational vaccine design against HCV through exploring the antibody response to this infectious agent. We implement a comprehensive study that will fill the critically important gap in technology and knowledge related to the mechanisms of antibody-mediated neutralization of HCV. An important focus of this study will be to translate this information to characterize the envelope structure of the virus and to develop new vaccine strategies. In another line of research we aim to contribute to understanding the pathogenesis of HCV infection and its effect on the mechanisms

		leading to hepatocellular carcinoma (HCC). We study the dynamic evolutionary balance between the viral modulations of epigenetic changes of chromatin, the HCC-borne mutations, the viral genome and immune system. We also explore the processes that drives HCV infected hepatocytes towards becoming invasive and metastatic.
Dr. Meir Shamay	Viral oncology	The research interests in the lab are to study the functional interactions between viral proteins and the cellular machinery, which control both the viral life cycle and tumorigenesis. The viruses we study are the human gamma herpes viruses; Kaposi's sarcoma associated herpesvirus (KSHV, HHV-8) and Epstein-Barr virus (EBV, HHV-4) that are associated with increasing number of human malignancies. The goal of our lab is to expand our knowledge on viral infections, and to utilize this knowledge for the development and use of drugs that specifically target virally infected cells.
Dr. Hava Gil-Henn	signal transduction	Research in our laboratory focuses on signal transduction mechanisms in health and disease. We focus on signaling mechanisms which control variable processes such as cancer metastasis, cell migration and invasion during wound healing, brain and behavior, and neurodegenerative disease. We use a multidisciplinary approach, which combines advanced molecular and cellular biology methods, in vitro and in vivo RNAi-mediated genetic manipulations, transgenic and knockout mice models, cutting edge in vivo methods, high-resolution fluorescent and intravital imaging, high-throughput proteogenomic and bioinformatic analysis. Using these methods, we are trying to understand and characterize, at the molecular, cellular, and whole organism levels, the signaling networks and mechanisms that regulate cancer metastasis, wound healing, and brain function in health and disease. We apply the knowledge gained from our interdisciplinary studies into new strategies for

		diagnosis and therapeutics of cancer metastasis and brain disorders.

Structural Biology and Drug Design

PI's name	Research scope + link to group's website	Brief research description
Prof. Avraham Samson	Drug Discovery	**Development of computational tools for drug design** To assist drug design, we are developing computational tools to predict ligand binding sites. In the past, we developed a structure based program using normal mode accompanied exposure changes to predict ligand binding sites with 90% accuracy. As one would expect we are currently attempting to increase the accuracy to 100%. In addition, we are developing ligand optimization programs based on local motion in the binding site. In particular, we are optimizing drugs which bind to acetylcholine receptors, and acetylcholine esterases, and improve concentration in patients with Alzheimer's and dementia. **Calculation of biomolecular motion and correlation with biological activity** To capture the motion involved in biological mechanisms, we are developing computational tools using molecular dynamics and normal modes. With these tools, we were able to calculate the motion associated with channel opening of the acetylcholine receptor, and show how this motion is inhibited by binding of snake toxin. In addition, we could calculate the conformational change exhibited by prion proteins and show the infection propagation in the mad cow disease. We are currently calculating motion of various biomolecules such as HIV glycoproteins, enzymes, receptors, channels, and the ribosome to explain biological activity.

		Development of novel therapies for Alzheimer's disease To develop viable therapies for Alzheimer's disease, we are testing promising drug candidates such as arginase inhibitors. First, we administer the drug candidates in mice suffering from Alzheimer's disease. Then, we test their effect on memory and learning, using behavioral experiments such as Morris water maze, and fear conditioning. Finally, we test their effect on brain morphology, using immunohistological tools. If a drug candidate improves memory and learning, and it also reduces inflammation and amyloidosis, then we move on to clinical trials in human patients suffering from Alzheimer's disease.
Dr. NirQvit	Protein–Protein Interactions	Protein–protein interactions represent a significant proportion of functionally relevant biological interactions, and therefore manipulating these interactions is an important therapeutic strategy. The main focus of the Qvit lab is the identification of molecularmodulators of protein-protein interaction using bioinformatics analysis, peptide and protein chemistry, and system-wide biological assays. Our goal is the development of compounds capable of modulating protein complexes that will allow better understanding of the role of specific protein-protein interactions in cells and will be a starting point for the development of therapeutic compounds.
Dr. Ronit Ilouz	Molecular and Cellular Mechanisms regulated by Kinases in health and disease	The project idea is to translate the genomic data into a three dimensional structure to enable a better understanding of the molecular and cellular mechanisms, and then to control it with a specific and precise drug targeting therapy based on the SNP mutation. Aberrant Protein Kinase A (PKA) localization has been linked to a Parkinson disease. The diagnosed patients have Single Nucleotide Polymorphisms (SNPs) in the PKA_ RIβ gene. The

		lab is integrating various methods including X-ray crystallography and advanced microscopy techniques as well as molecular biology, biochemistry and signal transduction. Elucidating the cellular and the molecular interactions that are properly controlled by PKA signaling and are dysregulated in the neurodegenerative disease will help discover opportunities and challenges toward personalized medicine.
Dr. Moshe Dessau	Structural Biology of Infectious Diseases	In our lab we use structural and biophysical approaches for studying the organization and dynamics of macromolecular assemblies. Our research focuses on determining how protein structure and interactions guide the principles and mechanisms of viral and parasitic infection. Our main emphasis is on third-world and poverty related emerging pathogens. These neglected diseases are growing concern in many developing countries as well as in the rest of the world. Nevertheless, their prevalence throughout the world is yet to be reflected in research agenda and resources allocation. Thus, developing communities face vast obstacles in fighting these pathogens that induce illnesses with high mortality rates. We generally interested in two different systems: (1) How do viruses assemble and how do they enter the cells they infect? Can we exploit our structural understanding of viral entry with progressive methods in biophysics and cell biology to develop novel strategies for vaccine design? (2) What are the unique structural features of eukaryotic parasites? How can we exploit structural investigation of unique biological processes in eukaryotic parasites to design novel therapeutics?

Developmental Biology, Regenerative Medicine, and Aging

PI's name	Research scope + link to group's website	Brief research description
Prof. David Karasik	Genetics of Musculoskeletal Disease	The Lab's research focuses on the heritable musculoskeletal disorders of aging, such as osteoporosis, osteoarthritis, kidney failure, muscle loss (sarcopenia), and fatty infiltration of muscle and liver. Our search for genes underlying variation in risk of these common diseases, which began with the genome-wide association studies (GWAS) in human populations, is reinforced by validation using functional experiments in animal models (zebrafish) and mammal cells, based on homology between the species and evolutionary theory. We use bioinformatics tools and CRISPR-Cas9 technology for gene modifications and histology, RNA-Seq, western blot for protein and microCT imaging for musculoskeletal phenotyping.
Dr. Ron Piran	Diabetes research and regenerative medicine	Our lab is developing methods for pancreatic beta-cell regeneration as an approach to treat diabetes. Our goal is to replenish the beta-cell population in diabetic patients. Our strategy is to use drugs to convert neighboring alpha-cells into beta-cells in order to step up insulin production. We were successful using this approach in mice. Our efforts are directed towards increasing the conversion rate from alpha- to beta-cells in different diabetic models, with our growing knowledge of how the PAR2 receptor mediates this process. We are also attempting to stabilize the newly formed beta-cells by preventing their continued transdifferentiation into delta-cells. Regenerative medicine is not limited to beta-cells, and our findings are therefore relevant to other fields where regeneration therapy is needed. So far, our discoveries have been shown to have implications for the treatment of hepatitis and limb amputations.

Dr. David Enshell-Seijffers	Developmental Biology and Stem Cell Regulation	Stem cell therapy is considered to be the leading potential methodology to cure a variety of devastated diseases currently lacking treatment. However, while the intrinsic properties of stem cells are under intensive study, the comparatively rudimentary understanding of the role of the niche in regulating stem cell behavior has been an impediment to effectively integrating in vivo and in vitro studies to exploit the therapeutic potential of adult stem cells. Our research uses the hair follicle as a model system to study the molecular interactions between the stem cells and their microenvironment. We use sophisticated genetic methodologies in mice and exploit the accessibility of the hair follicle to reveal genetic networks that regulate stem cell activity.

The Microbiome

PI's name	**Research scope + link to group's website**	**Brief research description**
Dr. Omry Koren	Microbiome and Microbiology	Our research focuses on the microbiome, studying the roles of the trillions of bacteria that reside within each individual. We have a wide variety of research interests including interactions between microbiota and the host endocrine system, host behavior, and host development, in health and in disease states.

Genetics, Chromatin Structure and Nuclear Organization

PI's name	**Research scope + link to group's website**	**Brief research description**

Dr. Itay Onn	Chromosome Instability and Dynamics	Three dimensional organizations have been identified as a highly important property of chromatin that ensures genome dynamics and integrity. Chromatin organization largely depends on protein complexes of the Structural Maintenance of Chromosome (SMC) family. However, the molecular basis of their activity is still elusive. In order to elucidate the mechanism by which SMC complexes organize chromatin,we use yeast as a model system and apply a multidisciplinary experimental approach that includes genetics, biochemistry, molecular and cellular biology, as well as advanced microscopy techniques. Research in the Chromosome Instability and Dynamics lab provides new insights into some of the most fundamental processes in cells and elucidates the impact of SMC complexes on human health.
Dr. Kobi Maman	Laboratory of genomic instability	Our lab combines sensitive, high-throughput, genomic assays, and computational modeling, in order to crack the genomic code that drives genome instability in different cell-types, pathologies and conditions, and to grasp the landscape of DNA lesions in cancer. We are particularly interested in the “double-edged swords” of the genome – physiological mechanisms that impose a threat on genome integrity, such as those involve in the formation of the immune repertoire, or the relief of DNA torsional stress. We investigate how these processes are targeted across the genome, how they are controlled, and what makes certain genomic sites more vulnerable than others to the “off-target” activity of these processes. Understanding this natural fragility of the genome will enable us to predict oncogenic events and to mark targets for cancer diagnosis and therapy
Prof. Amnon Harel	Nuclear Transport and Neurodegeneration	We study the molecular mechanisms underlying human neurodegenerative diseases involving drastic damage to the central nervous system. We

		identified novel disease-causing mutations in nuclear pore and nuclear envelope components. Patient cells and stem cell (iPSC)-derived cellular models are being used to link the clinical symptoms in patients with specific nuclear functions. We combine super resolution and electron microscopy with biochemical and genetic methods to study these topics.

Neurobiology

PI's name	Research scope + link to group's website	Brief research description
Dr. Evan Elliott	Neurobiology	The laboratory of neuroscience uses state of the art techniques to study neurodevelopmental disorders including autism spectrum disorders. Our main goals include to understand the biological mechanisms involved in autism spectrum disorders and to understand how epigenetic mechanisms affect behavior and neurodevelopment. Multiple techniques are used, including molecular techniques, whole throughput sequencing, and animal behavioral phenotyping. We also use human tissue samples, including brain samples, to compare to our findings in animal models of autism and other neurodevelopmental disorders.