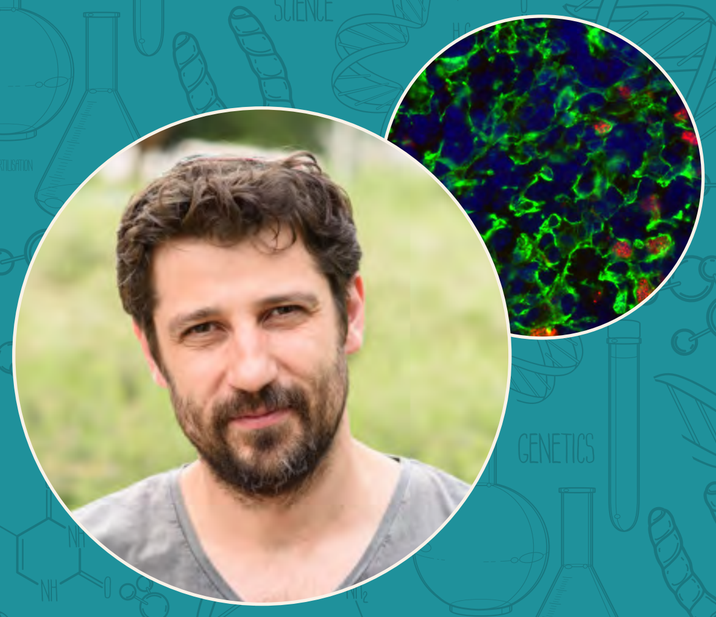
מכון ויצמן למדע

WEIZMANN INSTITUTE OF SCIENCE

LIFE SCIENCES LABS

Weizmann Institute of Science



Kobi Abramson

Immunology

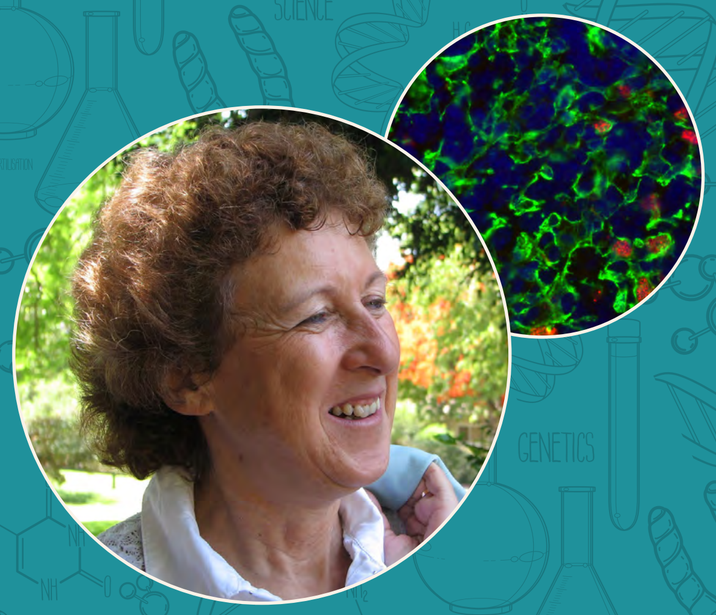
KEYWORDS

- Thymus
- Tolerance
- Autoimmunity
- T cells
- Cancer

WHAT	Immunological tolerance and autoimmunity
HOW	Functional genomics and transcriptomics in mouse models and humans
MODEL ORGANISM	Mice, Humans
MAJOR METHODS	Gene editing, gene knock-out, flow cytometry, RNA-seq, ATAC-seq.

Our research group is broadly interested in understanding how immunological tolerance to self is established in the thymus and how breakdown of this process results in autoimmunity.

In particular, we focus on a very unique population of the thymic stroma, called the medullary thymic epithelial cells (mTECs). Specifically, mTECs are endowed with an amazing and unique capacity to express, and subsequently present, essentially all body antigens, including those whose expression was originally thought to be restricted only to peripheral organs (e.g. insulin, casein, etc.). Such “promiscuous” expression of tissue-restricted-antigen (TRA) genes in the thymus “foreshadows” the self-antigens that T cells would encounter once they reach maturity and are released into the body.



Lia Addadi

Structural Chemical Biology

KEYWORDS

- Biomineralization
- Organic crystals
- Cholesterol
- cryo-FIB-SEM
- Biogenic photonic crystals

WHAT Biomineralization and pathological crystallizations

HOW We study processes by which organisms produce physiological or pathological mineral phases

MODEL ORGANISM Any organism from unicellular algae to humans, building interesting mineralized tissues

MAJOR METHODS 2D and 3D scanning cryo-electron microscopy, X-ray crystallography, confocal microscopy, micro-spectroscopy

We study the interactions and cross talk between crystals and biological environment, spanning several orders of magnitude from the molecular level to cell and tissue level. We focus on the ion pathways leading to the formation of mineralized tissues. Examples range from calcified coatings in green algae to sea urchin spines, to vertebrate bone. We focus on structure-function relations, in particular of unique optical devices in the eyes of mainly aquatic, but also terrestrial animals. We study cholesterol crystals in atherosclerotic plaques, trying to understand how they form and how they can dissolve.

Ariel Afek

Chemical & Structural Biology

WHAT Genome biophysics

HOW We investigate fundamental principles of mutagenesis and gene expression by high-throughput methods

MODEL ORGANISM Cell-free systems, Yeast, Mammalian cells

MAJOR METHODS High-throughput protein-DNA binding measurements,Mutagenesis assays, Computational genomics and modeling, Biochemistry and structural biology, Genetic manipulations

KEYWORDS

- Mutations and cancer
- DNA damage
- Protein-DNA recognition
- Mechanical and chemical DNA perturbations
- DNA structure

To understand and treat genetic diseases we need to decipher, at the molecular level, the biochemical processes that drive them; processes such as gene expression, DNA replication, and DNA damage repair.

Our goal is to obtain a deep molecular understanding of protein-DNA interactions involved in these fundamental processes, as well as their roles in physiology, disease, and evolution.

To accomplish this, we develop and use cutting-edge approaches to manipulate DNA molecules in high throughput and to introduce chemical and mechanical DNA perturbations that frequently occur in the genome.

We believe in a multidisciplinary view that closely integrates experimental and computational approaches.

Asaph Aharoni

Plant & Environmental Sciences

KEYWORDS

- Plant interactions
- Metabolic pathways
- Microbiome
- OMICS
- Chemical defense

WHAT

The role of specialized metabolism in plant- environment interactions

HOW

The lab has four expertise clusters (biology, chemistry, microbiology & computation) that use a unique infrastructure.

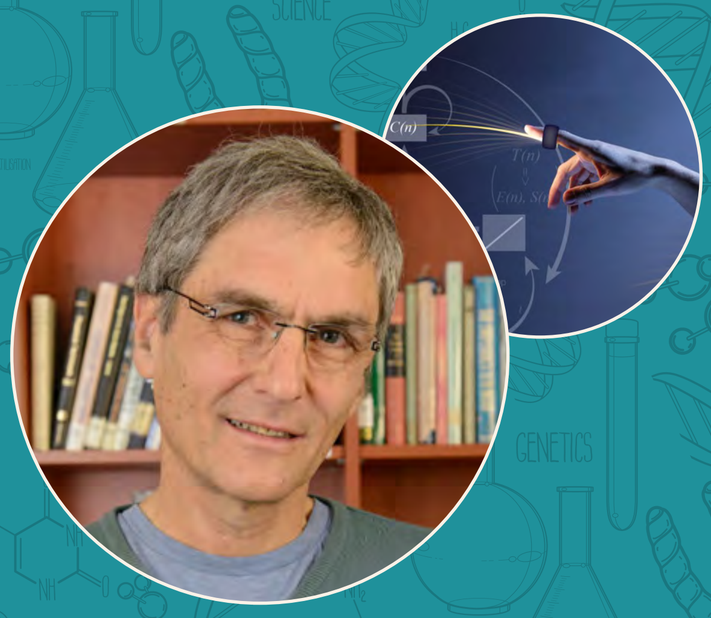
MODEL ORGANISM

Plants

MAJOR METHODS

- High resolution mass spectrometry (metabolomics; proteomics; mass spectrometry imaging; metabolite purification)
- Transcriptomics and proteomics
- Microbiome analysis
- Genome editing
- Metabolic engineering

The term ‘METABOLOME’ describes the complement of all metabolites expressed in a cell, tissue or organism during its lifetime. We aim at understanding how plants make and regulate a tremendous diversity of small molecules and the role of these chemicals in plant-environmental interactions (e.g. pigments, anti-fungal, bacterial, herbivory metabolites and systemic signaling molecules). We study plant metabolites and their impact on above ground interactions mediated through the plant outer surface layers as well below ground in roots, their secretions and interactions with rhizosphere organisms. Experiments are conducted both indoors and recently outdoors, in nature (using genome edited plants).



Ehud Ahissar

Neurobiology

KEYWORDS

- Closed-loop perception
- Active sensing
- Touch
- Vision
- Homeostasis

WHAT Brain Research

HOW We investigate how mammals perceive the world they live in and synthesize it in robots

MODEL ORGANISM Rats, humans, robots

MAJOR METHODS Electrophysiology, ethology, modeling, engineering, anatomy

What does it mean for a brain to perceive? What are the processes underlying the seemingly effortless acts of seeing, feeling, hearing, tasting or smelling? In our lab we try to answer some of these questions. We focus on the senses of touch and vision: we study them in rodents and humans, construct them in synthetic (robotic) and hybrid (brain-machine) agents, and substitute one with the other.

Ronen Alon

Immunology

KEYWORDS

- Inflammation
- Infection
- Cancer immunotherapy
- Transendothelial migration

WHAT

Leukocyte trafficking across blood vessels

HOW

We study in vitro and in vivo how specific trafficking signals are used by immune cells to reach sites of inflammation and translate this information into improved targeting of cancer killing immune cells to sites of metastasis

MODEL ORGANISM

Mouse and human

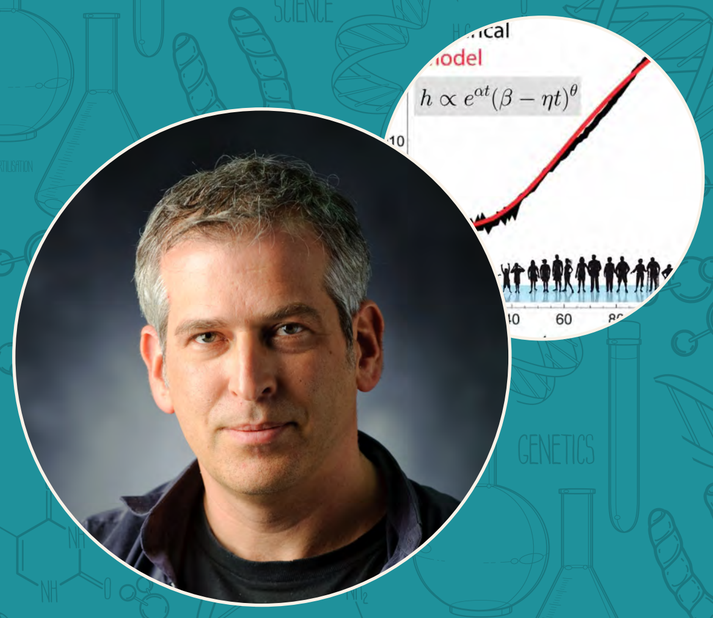
MAJOR METHODS

- Advanced imaging (light sheet microscopy, electron microscopy)
- Flow cytometry
- Genomic techniques
- Cancer and infection mice models

Circulating immune cells must exit blood vessels near specific target sites of injury, inflammation or tissue repair. The vessel wall at these sites displays specific combinations of traffic signals which operate to recruit specific circulating subsets with proper receptors to these signals. We use genetically manipulated mice, together with state-of-the-art imaging techniques, to dissect how these trafficking molecules promote context- and tissue- selective exit of immune cells through distinct blood vessels.

We also study how chemotactic and antigenic signals promote the stoppage of lymphocytes on dendritic cells during distinct infectious processes. We follow how specific subsets of lymphocytes use specific adhesion signals to undergo differentiation into efficient effector and memory cells.

A new avenue of research in our lab focuses on the trafficking mechanisms used by tumor specific T cells to enter metastatic lesions at various target organs, in particular the lungs. This information is critical for improved targeting of genetically-engineered tumor-specific T cells to sites of lung metastasis.



Uri Alon

Molecular Cell Biology

KEYWORDS

Cells

Circuits

Biology

WHAT	System Biology
HOW	Design principle of Biological circuits. Ageing and Age-related disease
MODEL ORGANISM	human
MAJOR METHODS	System Biology, Mathematical Modeling, Molecular Biology

Understanding biological circuits that perform computations is a central problem in biology. Circuits can be made of proteins inside the cells, or cells that communicate with each other in a tissue. Our lab studies biological circuits using a combined experimental and theoretical approach, aiming to uncover general underlying principles that govern their functioning and evolution. Current projects in the lab focus on the role of senescent cells in human ageing, mortality and diseases incidence, principles of hormone circuits, origins of autoimmune diseases, origins and timescales of mood disorders, inflammation and fibrosis.

Ido Amit

Immunology

KEYWORDS

- Single cell genomics
- Cancer
- Neurodegeneration
- Immunometabolism
- Autoimmune
- CRISPR

WHAT

Applying advanced genomics and big data approaches to characterize the immune system and develop new immunotherapies

HOW

Our lab is a major driver in developing and applying cutting edge single-cell genomics technologies and advanced computational approaches. We apply these novel tools in animal models and human patients to uncover immune regulatory mechanisms and pathways in cancer, neurodegeneration, autoimmune and metabolic disease.

MODEL ORGANISM

Mouse, human

MAJOR METHODS

Single cell genomic technologies, CRISPR and other genome engineering methods, modeling and computational analysis

We are world leaders in developing single-cell genomic technologies and their application in immunology and medicine. Our lab pioneered the field of single cell genomics. Using these technologies, we revealed cellular localization, clonality, cell-cell interactions, signaling and regulatory circuits determining immune activity. These powerful single-cell tools enable us to uncover novel cell types, pathways and targets of immune regulation in the fields of development, cancer, metabolism, autoimmunity and neurodegenerative diseases. Together these unique technology and knowhow enable us to develop the next generation of immunotherapies.

Yaron Antebi

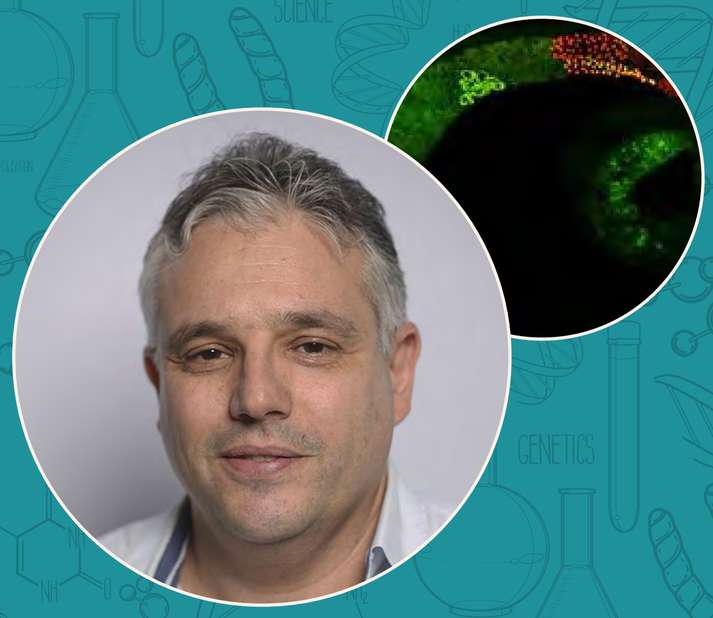
Molecular Genetics

KEYWORDS

- Cellular decision-making
- Cell-cell communication
- TGFβ superfamily
- Signal perception
- Systems biology

WHAT	Cell communication
HOW	Systems level analysis of signal processing in cellular decision making
MODEL ORGANISM	Mus Musculus
MAJOR METHODS	Flow cytometry, Live cell microscopy, Tissure culture, Molecular biology, Mathematical models

Our lab studies cellular communication pathways that regulate differentiation and decision-making processes in cells, from a systems level perspective. We focus on the way extracellular information is perceived by individual cells and control their response. Using single cell quantitative tools, we study the encoding of the extracellular signals into few intracelluar mediators, and map the spectrum of responses generated by a large space of combinatorial cues. Combining experimental approaches with mathematical modeling, we generate predictive bio-physical models, providing a deeper understanding of these cellular processes



Eli Arama

Molecular Genetics

KEYWORDS

- Programmed cell death
- Caspases
- Drosophila
- Development

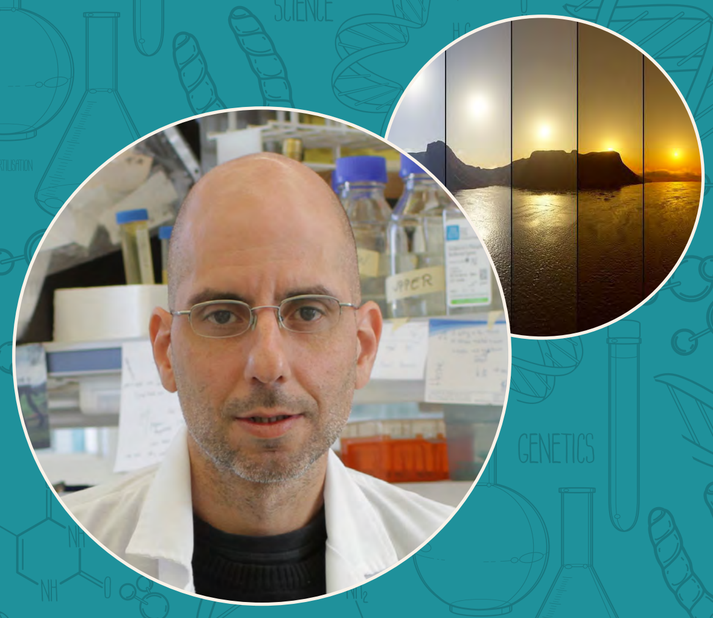
WHAT Programmed Cell Death and Cellular Destruction in Development

HOW Death without caspases and caspases without death in development

MODEL ORGANISM Drosophila melanogaster

MAJOR METHODS Genetics, microscopy/imaging, cell and molecular biology

Programmed cell death (PCD) is a regulated cell suicide process functions to eliminate unwanted or dangerous cells. Malfunction of PCD is associated with many diseases, including cancer and neurodegenerative disorders. Apoptosis, the most abundant form of PCD, is executed by proteases called caspases. However, activation of caspases does not always lead to PCD, and can promote a variety of non-lethal cellular processes (CDPs), whereas cell death can sometimes proceed in the absence of caspases by triggering alternative cell death pathways (ACDs). We discovered and study several developmental paradigms of CDPs and ACDs, with the aim of addressing some of the key questions in the field.



Gad Asher

Department of Biomolecular Sciences

KEYWORDS

- Circadian clocks
- Metabolism
- Exercise biology
- Mitochondria
- Oxygen

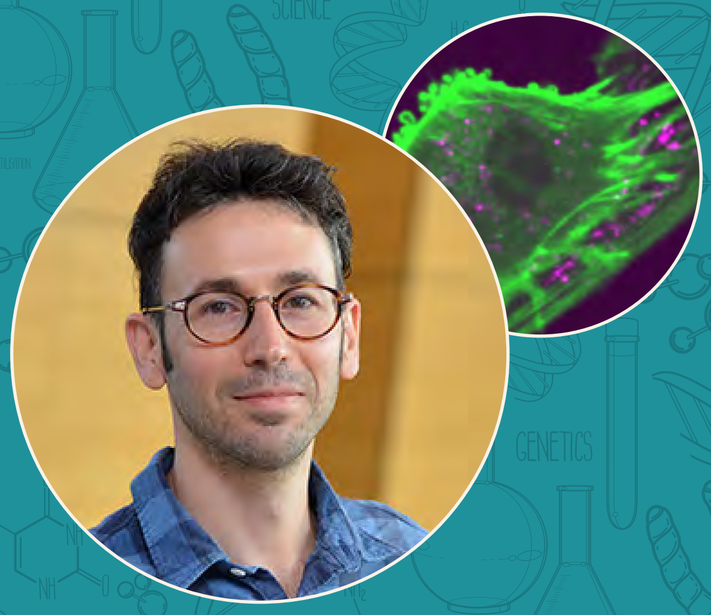
WHAT Circadian Clocks & Metabolic Rhythms

HOW Study clock interactions with metabolism & the environment

MODEL ORGANISM Humans, Mice, Cyanobacteria, Cell Culture

MAJOR METHODS Molecular Biology, Biochemistry, Genomics & Metabolomics, Live-imaging, Physiological & Behavioral measurements

Our physiology and behavior are subject to daily oscillations that are driven by an endogenous circadian clock. Our main research interest is to identify daily metabolic cycles in mammals and mechanistically address their interplay with circadian clocks. Specifically, we are interested in the interaction between oxygen metabolism, mitochondrial function and exercise biology in the context of circadian rhythms. To this end, we employ a diverse arsenal of experimental approaches ranging from biochemical and molecular biology methods through in vivo imaging in cultured cells and living animals to metabolomics analysis and animal behavioral studies.



Ori Avinoam

Department of Biomolecular Sciences

KEYWORDS

- Membrane fusion
- Cell-to-cell fusion
- Membrane ultrastructure
- Membrane Homeostasis
- Trafficking

WHAT Molecular Membrane Biology

HOW We seek a molecular understanding of membrane remodeling and its contribution to health and disease.

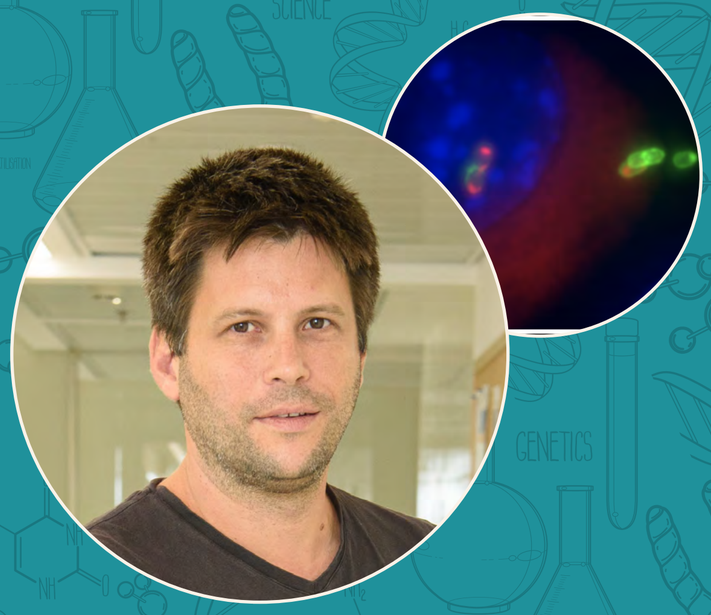
MODEL ORGANISM Cell lines, Primary cultures, Drosophila melanogaster, Caenorhabditis elegans

MAJOR METHODS Live-Imaging, 3D Electron Microscopy, Correlative-Light and Electron Microscopy, Molecular Cell Biology.

Biological membranes are universally conserved dynamic structures that constantly change their shape and composition to drive biological functions.

We are interested in understanding how cellular membranes gain their exquisite architecture and how subdomains of the membrane can be reshaped into functional structures that allow the trafficking of material and information in and between cells (e.g. endocytosis, exocytosis, exosomes). We are also fascinated by the process of cell-to-cell fusion, which is necessary for innumerable developmental processes such as fertilization, and myogenesis.

To gain previously inaccessible insight into the molecular mechanisms and physiological functions of membrane remodeling, we take a multimodal imaging approach combining several advanced imaging techniques including total internal reflection fluorescence microscopy (TIRF-M), confocal microscopy and correlated light and electron microscopy (CLEM), which we apply to a variety of cell culture and in vivo model systems.



Roi Avraham

Biological Regulation

KEYWORDS

- Systems biology
- Immunology
- Microbiology
- Infectious disease

WHAT Host-pathogen interactions

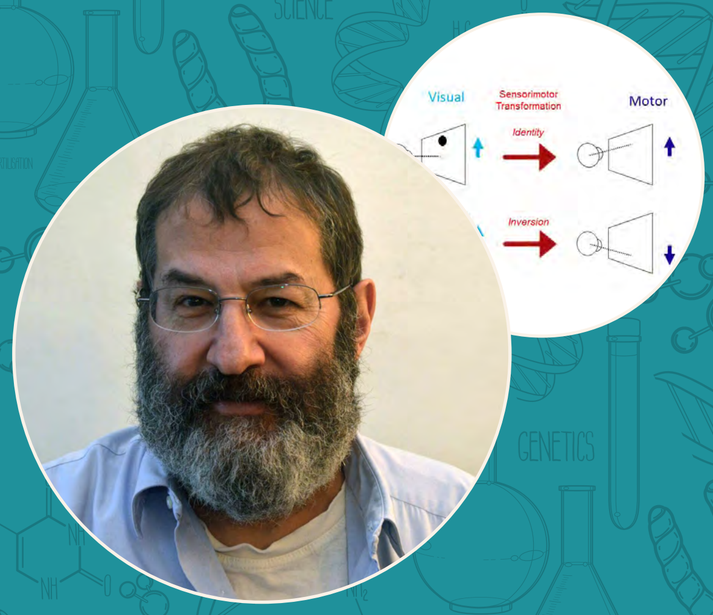
HOW Our lab studies how individual encounters between host and pathogenic bacteria ultimately define the outcome of infection

MODEL ORGANISM Human and mouse immune cells, *Salmonella Typhimurium*

MAJOR METHODS Single cell RNA-seq, Metabolomics, imaging, FACS, bioinformatics

By applying cross-disciplinary single-cell analysis platforms that collectively enable us to extensively profile and precisely monitor host-pathogen interactions within the context of in vivo infections, we aim to answer these Main questions:

- How bacteria regulate different virulence strategies to optimize pathogenicity in the host environment.
- How do innate immune cells recognize pathogens, integrate signals from bacterial ligands and determine cell fate.
- Ongoing improvement of the methodologies we apply to study host-pathogen interactions.
- Characterize the in vivo landscape of human infection at a resolution of individual host-pathogen encounters: why do some get sick and some don’t?



Shabtai Barash

Neurobiology

KEYWORDS

- Eye movements
- Sensorimotor transformations
- Attention
- Fatigue
- Working memory

WHAT Neurophysiology

HOW Neuroscience of looking: bridging body, brain, and mind

MODEL ORGANISM Humans; by collaboration also monkeys

MAJOR METHODS Studying behavior in controlled conditions – gaze direction, autonomic measures, more. Other methods as fitting

My primary interest is with saccadic eye movements. We can see detailed images only at the line of gaze. We thus can see in detail only serially, one object after another. To shift the line of gaze we make a saccadic eye movement; this is a fundamental design principle of primate vision. Many issues concern saccades; here are some open for study. (1) Fatigue in looking. (2) Interactions of the readout from visual and motor working-memories with the flow of sensation. (3) Communication by eye-contact and influence of emotion on looking. (4) Looking at night, while the line of daytime gaze is blind. (5) Changes of looking in disease (eye, brain, ‘mental’).

Naama Barkai

Moleuclar Genetics

KEYWORDS

- Systems biology
- Development
- Bioinformatics
- Transcription
- Replication
- Chromatin

WHAT

Systems Biology

HOW

- Biological circuits: design, function and evolution
- Regulatory genome: transcription, replication and the chromatin as a communication platform
- Developmental patterning: morphogen gradients, scaling, robustness

MODEL ORGANISM

S. cerevisiae
Drosophila (in collaboration)

MAJOR METHODS

- Computation modeling
- High-throughput sequencing-based mapping and bioinformatics
- Genetic manipulations, molecular biology
- Microscopy
- (a touch of) biochemistry

Cells are constantly "making decisions" - monitoring their environment, modulating their metabolism and 'deciding' whether to divide, differentiate or die. For this, they use biochemical circuits composed of interacting genes and proteins. Advances over the past decades have mapped many of these circuits. Still, can we infer the underlying logic from the detailed circuit structure? Can we deduce the selection forces that shaped these circuits during evolution? What are the principles that govern the design and function of these circuits and how similar or different are they from principles that guide the design of man-made machines? The interplay between variability and robustness is a hallmark of biological computation: Biological systems are inherently noisy, yet control their behavior precisely. Research projects in our lab quantify biological variability and identify its genetic origins, examine how variability is buffered by molecular circuits and investigate whether variability can in fact be employed to improve cellular computation. We encourage a multi-disciplinary approach, combining wet-lab experiments, dynamic-system theory and computational data analysis.

Avri Ben-Zeev

Molecular Cell Biology

KEYWORDS

- Wnt/β-catenin signaling
- Colon cancer
- Cell adhesion
- Motility and invasion

WHAT	Cancer Cell Biology
HOW	Adhesion-mediated signaling during cancer development and metastasis
MODEL ORGANISM	Human colon cancer cell lines Mouse models for metastasis Human colon cancer tissue
MAJOR METHODS	Transcriptomics, proteomics and secretomics Adhesion, motility and invasion Immunohistochemistry of tissues Gene and protein expression analysis

Cell-cell adhesion is a key biological process in multicellular organisms. We study the signals conveyed by cell-adhesion receptors that regulate gene expression. A tight coordination between cell adhesion and gene expression is found in normal tissues and this coordination is altered in invasive cancers.

We are investigating the Wnt/β-catenin pathway, because β-catenin has a dual role: as a major linker of cell adhesion receptors to the cytoskeleton, and as a key transducer of Wnt signaling to the nucleus where β-catenin activates target genes. Hyperactivation of this pathway is found in colon cancer. We are studying β-catenin target genes activated in colon cancer, especially those of the colonic stem cell signature and genes related to epithelial-mesenchymal transition. Our studies will shed light on both intestinal homeostasis and on development of metastatic colon cancer.

Moran Shalev-Benami

Structural Biology

KEYWORDS

- Membrane receptors
- GPCRs
- Cellular communication
- CNS
- Signaling

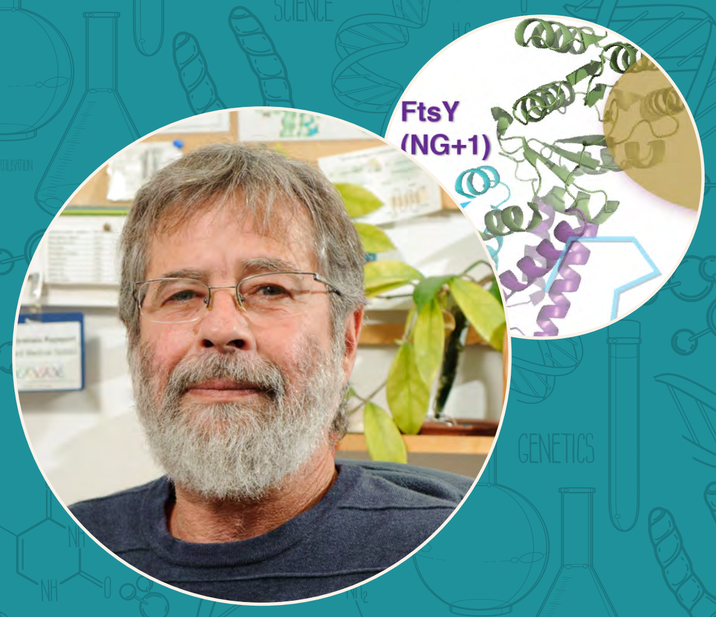
WHAT Cell-cell communication in the CNS

HOW Uncovering the structures of CNS receptors to understand their function through cryo-EM

MODEL ORGANISM Mammalian and Insect cells

MAJOR METHODS Cryo-EM; Microscopy; Biochemistry; Structural Biology; Single particle;

Macromolecular machineries residing within our cells mediate every aspect of cellular physiology in both health and disease. These machineries adopt complicated three-dimensional (3D) structures that are critical to their function. Our lab focuses on visualizing the complex architectures of macromolecular assemblies, with the aim of learning how their complicated structures contribute to their ability to mediate cellular functions. To do this we use a combination of structural, biophysical and biochemical techniques with an emphasis on high-resolution electron cryo- microscopy (cryo-EM).



Eitan Bibi

Biomolecular Sciences

KEYWORDS

- Signal Recognition Particle (SRP)
- FtsY
- SecYEG
- Membrane ribosomes
- MdfA

WHAT Ribosomes associated with the cytoplasmic membrane

HOW How do ribosomes reach the membrane for membrane proteins translation and the role of the SRP

MODEL ORGANISM Escherichia coli

MAJOR METHODS In vivo cross-linking with unnatural amino acids; Ribosome profiling; high throughput mass spectrometry; Crystallization; Single particle cryo-EM

We are interested in questions related to membrane protein biogenesis, structure, and function.

Biosynthetically, structurally and functionally, membrane proteins must follow interesting, dedicated principles. For example, unlike soluble proteins, most membrane proteins are translated by membrane-bound ribosomes and then assemble and function inside the lipophilic environment of the membrane.

We ask how cells produce membrane proteins and how various structural determinants affect their function: (i) How ribosomes and mRNAs target the membrane for localized translation of membrane proteins? (ii) What dictates the fascinating capabilities of multidrug transporters?

Moshe Biton

Biological Regulation

WHAT	Gut Tissue Dynamics
HOW	Understanding epithelial stem and immune cell interactions
MODEL ORGANISM	Human or mouse organoids and tissues
MAJOR METHODS	Organoids culture, co-culture of stem-immune cells, single-cell genomics, mouse and tissue biology, molecular biology

KEYWORDS

- Organoids
- Single-cell genomics
- Tissue Immunology
- Molecular Biology
- Tissue homeostasis

Signals arriving from the outside world play a key role in shaping a tissue. Disruption of the cellular equilibrium within the gut tissue may lead to various diseases, including food allergies, inflammatory bowel diseases, and cancer. To understand the intestinal tissue physiology at higher resolution, we are leveraging single-cell genomics and traditional experimental methods. We aim to decipher the role of epithelial - immune interactions in homeostasis and gut pathologies by 3D organoids, mouse and human samples. Our goal is to understand tissue basic principles and identify disease key pathways.

We focus on:

1. Epithelial stem cell biology.

2. Epithelial – immune interactions.

3. Inflammatory bowel diseases.

Rony Dahan

Immunology

KEYWORDS

Immunotherapy

Antibodies

Fc Receptors

WHAT Cancer Immunology and Immunotherapy

HOW We aim to develop novel translational strategies that will improve immunity against cancer, and to optimize the potency of currently available antibody-based immunotherapies

MODEL ORGANISM Human, mice

MAJOR METHODS Antibody Engineering, in vivo tumor models

The ability of antibodies to detect pathogens and malignant cells, and trigger diverse immune effector functions make them central players in the immune response. Monoclonal antibodies have turned into a powerful drug platform at the front of cancer immunotherapy approaches. Our group studies the mechanisms that control the activity of both natural and therapeutic antibodies.

We are particularly interested in the roles of the Fc regions of these antibodies and in their various Fcγ Receptors (FcγRs) in mediating anti-tumor activities,

For maximum clinical relevance we are studying human antibodies in mice humanized for FcγRs and other relevant human genes. We are exploring strategies to enhance the identified pathways and aim to create 2nd generation antibodies with improved activity.

Rivka Dikstein

Biomolecular Sciences

KEYWORDS

Spt5

Transcription elongation

Huntigton's disease

Translation initiation

Cancer

WHAT Precision and connectivity in gene regulation

HOW Investigating how transcription and translation control the cellular response to environmental stimuli

MODEL ORGANISM Mammals

MAJOR METHODS Molecular biology, biochemistry, genome-wide transcriptomic and translatomic, drug screening, CRISPR-Cas9

Regulation of transcription and mRNA translation is fundamental to all biological activities and is frequently altered in diseases. Our broad research interests are (i) to elucidate how transcription and translation control the cellular response to environmental stimuli; (ii) to reveal the connections between these processes and (iii) to develop drugs to manipulate these processes for potential treatment of cancer, chronic inflammation and neurodegenerative diseases. We address these issues utilizing several biological systems:

- Spt4/Spt5 (DSIF), a transcription elongation factor involved in stress responses and neurodegenerative diseases
- Regulation of translation initiation by TISU (a transcription and translation regulatory element), stress and mitogenic signals
- RNA modifications as mediators of the crosstalk between gene expression stages

Ron Diskin

Chemical & Structural Biology

WHAT

The interplay between viruses, cells, and the immune system

HOW

Structure function investigations of viral glycoproteins, antibodies and viral cellular receptors

MODEL ORGANISM

MAJOR METHODS

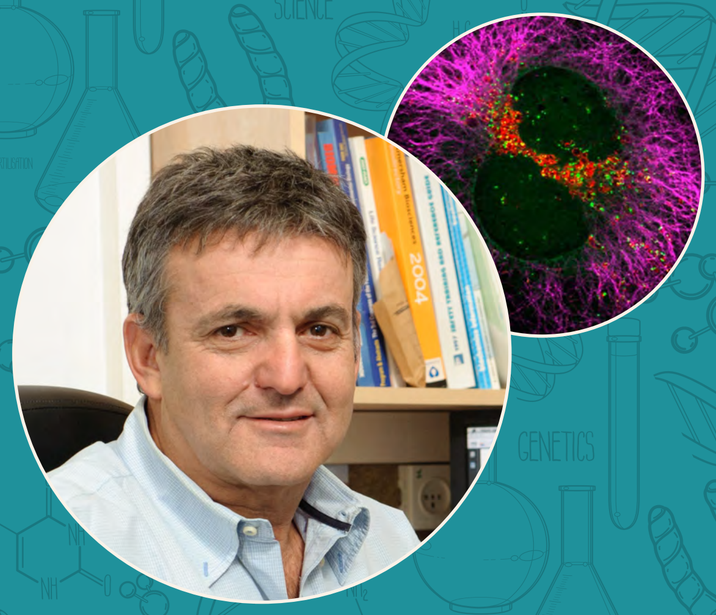
- X-ray crystallography
- Single particle cryo-EM
- Cell-based assays

KEYWORDS

- Viral infection
- Immunotherapy
- Molecular recognition
- Molecular Structure

Our research group investigates how viruses infect cells, how the immune system combats viral infections, and how viruses evade effective immune responses.

We take a structural biology approach to address these questions. We elucidate the molecular structures of key viral proteins, investigate how they attach to and utilize various cellular receptors. We also examine the potential of a humoral immune response to combat viral infections and design novel immunotherapeutic reagents. We focus on enveloped viruses in general, emphasizing viruses from the Arenaviridae family that contain some notorious human pathogens



Zvulun Elazar

Biomolecular Sciences

KEYWORDS

- Autophagy
- Membrane trafficking
- Neurodegeneration
- Microscopy
- Yeast

WHAT

Autophagy and Intracellular Membrane Trafficking

HOW

Study the mechanism and regulation of autophagosome biogenesis and maturation, the selective sequestration of novel cargo and the physiological implications of the pathway in health and disease – with emphasis on neurodegeneration and cancer.

MODEL ORGANISM

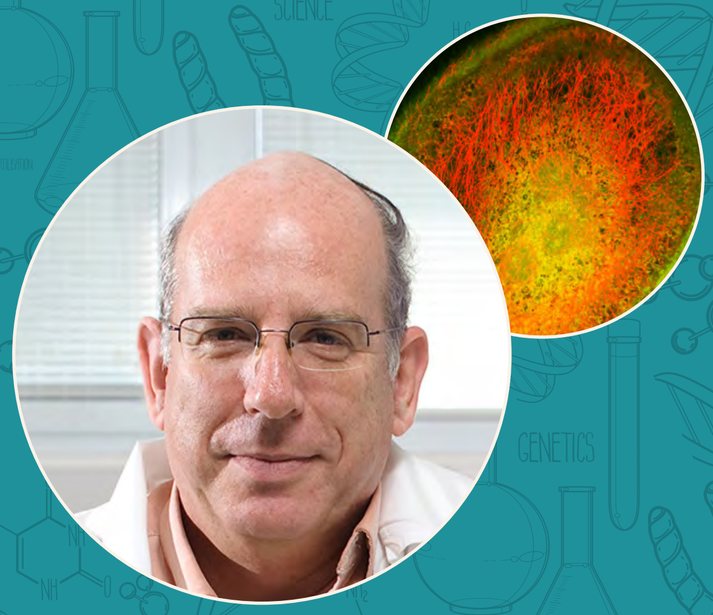
Human, Mouse, Yeast

MAJOR METHODS

Live confocal fluorescence microscopy, mouse physiology, mammalian cell culture, high-throughput screens, in vitro assays

Intracellular protein transport in membrane-bound vesicles is fundamental to cell physiology. Autophagy is a unique, highly conserved membrane trafficking pathway for degradation of excess or damaged macromolecules and organelles. It is induced by stress and implicated in apoptosis, cancer, infection and neurodegeneration.

In our lab we study the mechanism of autophagy and its role in health and disease, using mouse models, mammalian cell lines and budding yeast. Particular interests include elucidation of cargo-specific sequestration processes, establishment of mouse models for autophagy in neurodegeneration, and dissection of conserved mechanistic aspects by novel assays yeast genetics.



Ari Elson

Molecular Genetics

KEYWORDS

- Osteoclast
- Osteoporosis
- Genetic disease
- CRISPR
- Bone
- Osteopetrosis

WHAT Bone-degrading osteoclasts in health and disease

HOW We study how osteoclasts, the only cells in our body that can degrade bone, are formed and how they function, both in health and in disease

MODEL ORGANISM Mouse

MAJOR METHODS CRISPR, mouse models of diseases, molecular biology, biochemistry, genome-wide transcriptomics

The material that makes up the bones in our bodies is constantly being produced by osteoblasts and being degraded by osteoclasts (OCLs), the only cells in our bodies that can fulfill this function.
Balancing between bone production and degradation is essential for health and development. Excess OCL activity causes bone loss in, for example, osteoporosis and cancer, while loss of OCL activity causes the lethal genetic disease osteopetrosis.

Our goal is to understand the molecular and cellular mechanisms that drive and regulate the formation and function of OCLs in the context of health and in diseases. We aim to advance the basic knowledge of OCLs and bone biology, as well as to identify new targets, pathways, and strategies to treat bone disease.

Our studies encompass the molecular, cellular, and whole-animal level.

Eran Elinav

Immunology

WHAT — Host Microbiome interactions; innate immunology

HOW — Host-microbiome interactions in health and disease

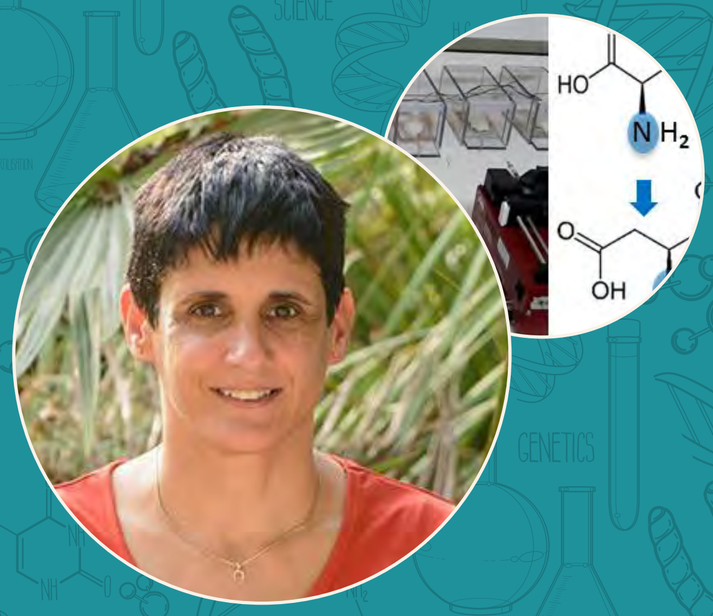
MODEL ORGANISM — Mouse, human

MAJOR METHODS — Next generation sequencing; germ-free experimentation; metabolomics; culturomics; human trials

KEYWORDS

- Microbiome
- Metabolism
- Infection
- Cancer
- Innate Immunology

The mammalian intestine contains trillions of microbes, collectively termed the microbiome. Dysregulation of host-microbiome interactions predisposes to disease ranging from chronic inflammation, obesity, the metabolic syndrome and even cancer. The Elinav lab mechanistically studies in mice and in humans the factors participating in the reciprocal regulation between the host and the intestinal microbial ecosystem, using advanced genomics, metabolomics, proteomics, mouse and human experimentation. Understanding the molecular basis of host-microbiome interactions may lead to development of new microbiome-targeting treatments.



Ayelet Erez

Biological Regulation

KEYWORDS

- Metabolism
- Cancer
- Nitrogen homeostasis
- Translational implications

WHAT	Metabolism
HOW	We identify metabolic changes that accompany or cause systemic diseases as cancer
MODEL ORGANISM	Human patients and mouse disease models, cell lines
MAJOR METHODS	Mass spectrometry, HPLC, isotopic tracing in vitro and in vivo

Our lab deciphers the dynamics of cellular metabolism at different disease states. In particular, we are interested in understanding the contribution of the urea cycle components to the metabolic changes that accompany disease pathogenesis. Urea cycle metabolites serve as metabolic junctions that directly contribute to distinct metabolic fluxes at different cellular states. Consequently, changes in the function of urea cycle proteins have important effects on cell growth, survival and proliferation. Identifying specific metabolic alterations during disease can potentially improve diagnosis, monitoring of progression, and therapeutic interventions.

Yuval Eshed

Plant & Environmental Sciences

KEYWORDS

- Flowering
- Florigen
- MADS
- Regulation

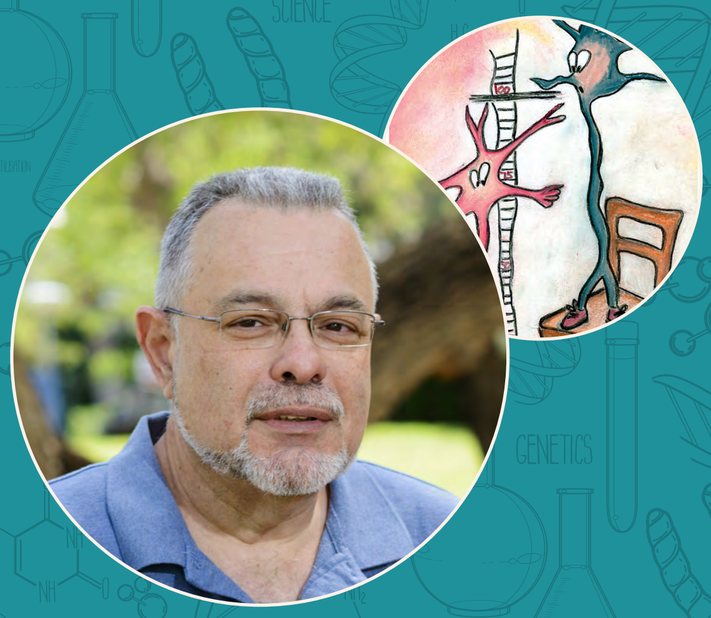
WHAT Plant Developmental genetics

HOW Mechanisms of tomato shoot apical meristem floral transition

MODEL ORGANISM Tomato

MAJOR METHODS Classical and genome editing aided genetics, expression profiling, large scale expression analysis

Florigen is a systemic plant hormone produced in leaves and travels to apices to initiate flowering. In tomato, local production of antiflorigenic signals inhibit floral transition in a dose and position dependent manners. Hence, the florigen/antflorigen balance in each bud determines if it will flower or, remain vegetative. Together, the two opposing hormones comprise a regulatory system that is environmentally tunable. We are looking for the direct targets of florigen by capturing the detailed events that follow its arrival to the target bud. In vivo genetic characterization of this process is used to understand the mechanisms underlying developmental transitions late in the plant life.



Mike Fainzilber

Molecular Neuroscience,
Biomolecular Sciences

KEYWORDS

- Cell size
- Axon regeneration
- Axonal transport
- RNA localization
- Local translation

WHAT Neuronal growth and nerve regeneration

HOW How are growth and size controlled in neurons and in other large cells?

MODEL ORGANISM Mouse

MAJOR METHODS Molecular biology, proteomics, neuronal cell biology, imaging, gene editing in mice

Neurons are the largest and longest cells in the body. How do neurons control their own growth, and what are the molecules or mechanisms that might allow their repair after injury? Can neurons sense their own size and length and how might they do that? Can we take advantage of such mechanisms to devise new approaches for repair and regeneration in the nervous system? Are mechanisms of size and growth control in neurons generalizable to other cell types? If these questions sound interesting, please get in touch.

Deborah Fass

Chemical & Structural Biology

WHAT Structural Biology

HOW Disulfide bonding in the assembly of complex extracellular biological materials such as extracellular matrix and mucins

MODEL ORGANISM Mouse, human

MAJOR METHODS X-ray crystallography, cryo-TEM, cryo-STEM tomography, biochemistry, enzymology

KEYWORDS

- Disulfide bonds
- Protein complex assembly
- Mucins
- Monoclonal antibody inhibitors
- Cancer

Our lab studies enzymes that catalyze the formation of disulfide bonds during protein folding and assembly. Our research combines structural and molecular biology with experiments in vivo, allowing us to determine how catalysts of disulfide bonding contribute to animal physiology and, in certain cases, pathology. Controlling the activities of disulfide catalysts may have applications in medicine and tissue engineering, an avenue we are pursuing through the design of specific inhibitors of these enzymes.

Sarel Fleishman

Biomolecular Sciences

KEYWORDS

- Protein structure
- Stability
- Catalytic efficiency
- PROSS
- FuncLib

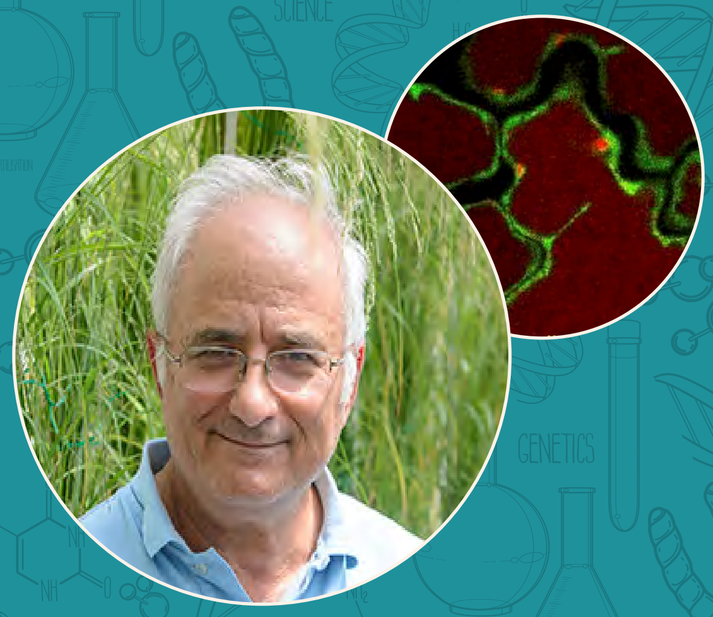
WHAT Computational protein design

HOW We develop algorithms for enzyme and antibody design and verify them using high-throughput experiments.

MODEL ORGANISM Designed proteins may come from any source organism

MAJOR METHODS Rosetta atomistic design; phylogenetic analysis; yeast display; high-throughput screening

Nature provides us with myriads of examples of exquisitely selective proteins that function as binders and enzymes. These proteins, however, are often formidably complex. For instance, a typical enzyme or the antigen-binding domain of an antibody comprise more than 200 amino acids and fold into complex three-dimensional conformations that depend critically on thousands of atomic interactions. By changing the protein sequence and structure or designing completely new proteins, we may generate desirable new enzymes for green chemistry, binders for research, diagnostics and therapeutics, and exquisite molecular sensors to measure metabolite concentrations. We develop methods for designing efficient and stable proteins with enhanced or new activities.



Robert Fluhr

Plant & Environmental Science

WHAT Plant Molecular Biology

HOW Plant adaptation to environmental stress

MODEL ORGANISM Arabidopsis

MAJOR METHODS Molecular biology, confocal microscopy, transgenic technology, bioinformatics, metabolomics

KEYWORDS

- Root growth
- Osmotic shock
- Biotic elicitors
- Proteases
- Drought

Pathogens and stressful environments rapidly induce reactive oxygen species (ROS) and activate cell death programs that include proteases and their inhibitors called serpins. We recently discovered a role for singlet oxygen, a special type of ROS that appears in many different stress reactions and activates cell death. Our research is meant to understand the origin the singlet oxygen, its effect and control so as to develop hardier plants.

Nir Fluman

Biomolecular Sciences

KEYWORDS

- Membrane proteins
- Folding
- Protein dynamics
- Degradation
- Chaperones

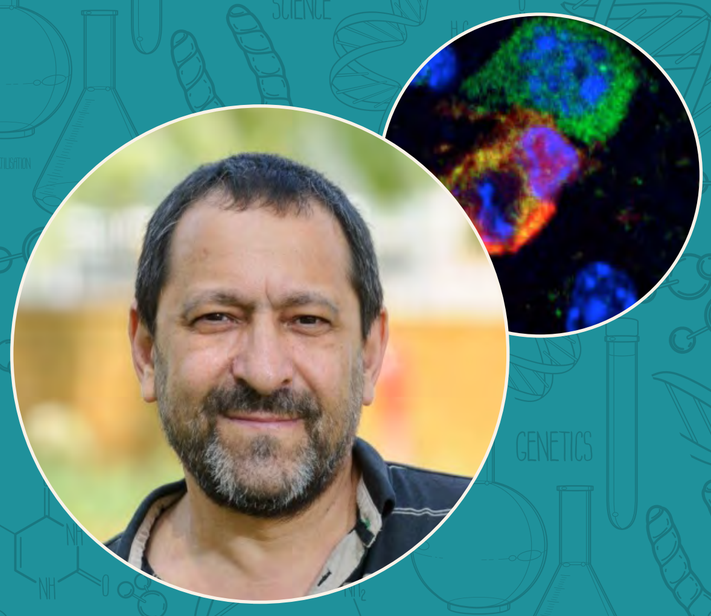
WHAT Membrane protein folding and quality control

HOW Illuminating how proteins fold in the membrane and how the cell handles them when they misfold

MODEL ORGANISM Escherichia coli, Human cell culture

MAJOR METHODS Protein Biochemistry, Genetics, Computational biology, Microbiology, Genomics

At any given moment, thousands of proteins are produced and need to fold in the cell. But folding is an incredibly complex process that very often fails, resulting in numerous devastating diseases. To deal with this challenge, the cell is equipped with an array of chaperones and proteases, performing quality control functions to safeguard the cell. We combine biochemistry and genetics with high throughput mutagenesis, robotics, and computational biology, to investigate how these events unfold for membrane proteins, which make up a quarter of the proteome in every living organism.



Tony Futerman

Biomolecular Sciences

WHAT Sphingolipids in Health and Disease

HOW Functional genomics, transcriptomics and proteomics in mouse model and humans

MODEL ORGANISM Mus Musculus, Homo Sapiens

MAJOR METHODS
Biochemistry
protein expression and imagining
Gene profiling and editing
Molecular dynamics

KEYWORDS

- Sphinglolipids
- ceramide synthase (CerS)
- Gaucher disease
- Parkinson’s disease

Our laboratory works on sphingolipids, important membrane components. We focus on two main areas: (i) sphingolipid synthesis and signaling, particularly of ceramide and (ii) sphingolipid storage diseases, with an emphasis on mechanistic understanding of disease pathology and also on therapeutic approaches.

Assaf Gal

Plant & Environmental Science

KEYWORDS

- Biomineralization
- Carbon cycle
- Ocean acidification

WHAT Mineral formation by phytoplankton

HOW We use advanced electron microscopy to understand the cellular processes of mineral morphogenesis

MODEL ORGANISM Diatoms, Coccolithophores

MAJOR METHODS Cryo electron microscopy, 3D electron tomography

Unicellular algae in the oceans are able to produce minerals in shapes and compositions unequaled by any manmade material. The biological mineralization process is intracellular and proceeds under strict cellular control, giving rise to spectacular morphologies of the mineral.

We study mineralization processes in two of the most abundant algal groups of modern oceans: 1) diatoms - that form cell wall made of nano-patterned silica, and 2) coccolithophores - that form calcium carbonate scales with unprecedented control over crystal morphology.

Our main tool is state-of-the-art electron microscopy that allow to follow these intracellular processes in 3D and with nanometer scale resolution.

Benny Geiger

Molecular Cell Biology

KEYWORDS

- Cell adhesion
- Invasive migration
- Epithelial barrier function
- Cancer immunotherapy

WHAT

Cell adhesion and migration

HOW

We study the molecular mechanisms underlying the adhesion of different cells (e.g. cancerous, immune, epithelial and osteoclasts) to neighboring cells and to the extracellular matrix

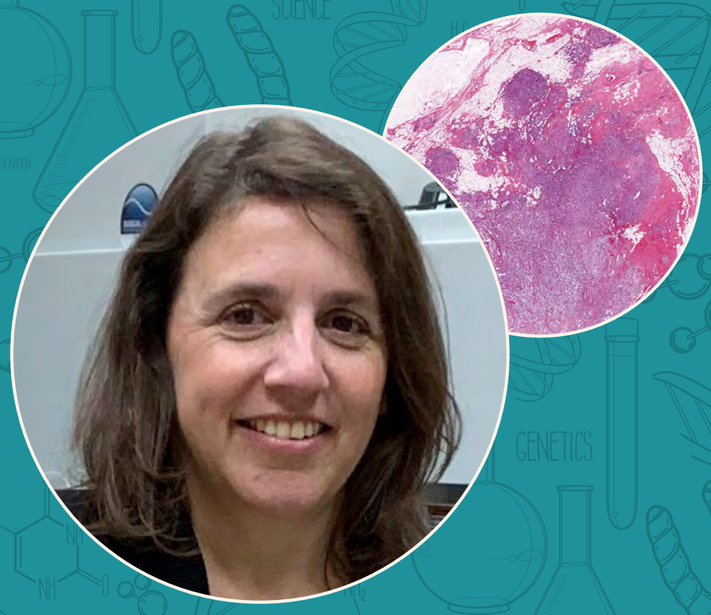
MODEL ORGANISM

Mostly cultured cells, mostly human

MAJOR METHODS

Advanced quantitative light and electron microscopy, gene manipulation technologies, engineering of cellular mictoenvironments

Adhesion to the extracellular matrix (ECM) or to neighboring cells regulates multiple cellular processes such as cell migration, morphogenesis, proliferation, gene expression and survival. Activation and regulation of these responses depends on multiple environmental cues, which are sensed and interpreted in specific cell-matrix and cell-cell adhesions. In our lab, we focus in particular on integrin- and cadherin-mediated adhesions, and study the mechanisms whereby they sense external surfaces, recognizing not only their chemical composition, but also their physical properties, including their topography, rigidity and ligand density. Systematic molecular modulation of the adhesion sites is used in an attempt to decipher the mechanisms whereby the adhesion-based molecular machinery integrates complex environmental information and triggers a coherent and robust response. Specifically, we combine a wide variety of molecular perturbation approaches with advanced, quantitative imaging technologies, to study cancer cell invasion and migration, osteoclast-mediated bone remodeling, platelet adhesion and activation, the formation and maintenance of the epithelial barrier function in the gut, the development of antigen-specific stimulatory surfaces that stimulate T-lymphocytes, and more.



Tami Geiger

Molecular Cell Biology

KEYWORDS

- Proteomics
- Cancer
- Immunotherapy
- System’s biology
- Metabolism

WHAT Clinical cancer proteomics

HOW We use mass spectrometry-based proteomics in order to elucidate tumor progression and drug resistance mechanisms

MODEL ORGANISM Human, Mouse

MAJOR METHODS Mass spectrometry, bioinformatics, immunohistochemistry, flow cytometry, molecular biology

Internal tumor heterogeneity is a major clinical challenge associated with tumor metastasis and treatment resistance. We aim to understand cancer complexity by combining mass spectrometry-based clinical proteomics, advanced computational analyses, and functional validations in-vitro and in-vivo. We further advance the proteomic technology and combine bulk tumor analyses with spatial and single cells analyses to decipher mechanisms of treatment resistance, that cannot be found using genomic approaches.

Jeffrey Gerst

Molecular Genetics

KEYWORDS

- RNA localization
- RNA-binding proteins
- Ribosome heterogeneity
- Organellar physiology
- Nanotubes

WHAT

Intracellular and Intercellular RNA trafficking

HOW

Intracellular and intercellular trafficking of mRNA and its role in protein localization and cell physiology

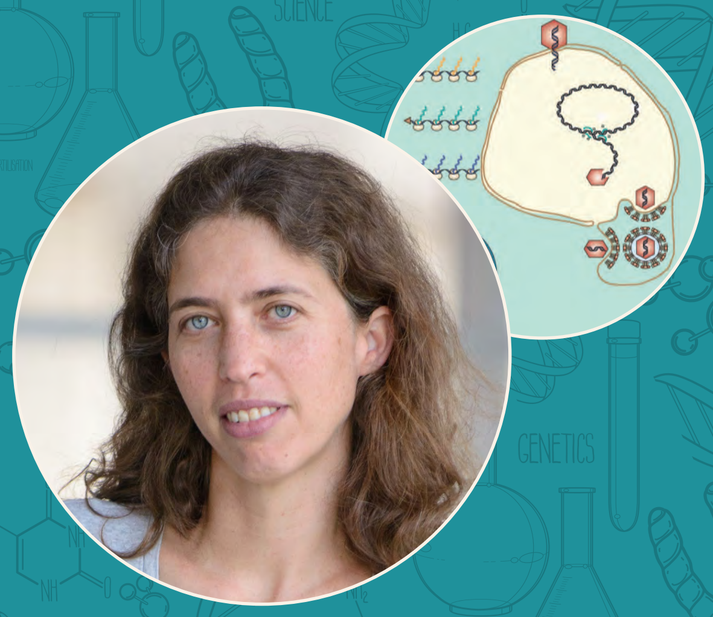
MODEL ORGANISM

Yeast, mammalian cells

MAJOR METHODS

- Live and single-molecule mRNA imaging
- Fluorescence microscopy
- RNA-seq and mass spectometry
- Yeast genetics
- Biochemistry

My lab studies the cell biology of RNA, namely how mRNA trafficking and localization are regulated and control basic cellular processes and cell physiology (e.g. protein translation, polarized growth, chemotaxis, mitochondria and peroxisome function, cell fusion, etc.). We use a wide variety of techniques, including fluorescence microscopy, RNA tagging and pull-downs, mass spectrometry, RNA-seq, whole translatome analysis, and genetic and biochemical techniques to understand the mechanisms involved. The work shows that mRNA trafficking and localized translation form a critical layer of organization within the cell responsible for protein localization and function.



Noam S. Ginossar

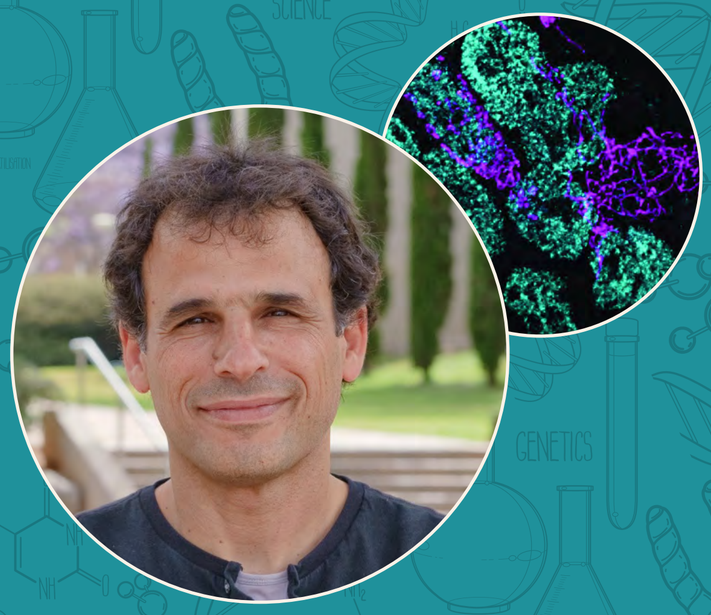
Molecular Genetics

KEYWORDS

- Viruses
- RNA biology
- Interferon
- latency

WHAT	Infection biology
HOW	Profiling viral infections
MODEL ORGANISM	Mammalian cells
MAJOR METHODS	• RNA-seq • Ribosome Profiling • CRISPR • Single cell RNA-seq • Molecular biology

We study viruses and we explore the creative strategies they use to maneuver their host cells. We are interested in deciphering the roles different viral elements are playing during infection, as well as how viruses interface with and commandeer cellular pathways to control gene expression. We study these complex interactions using mainly cytomegalovirus (CMV), a herpesvirus that infects the majority of the world's population, leading to severe diseases in newborns and immunocompromised adults. We anticipate that our studies will uncover new aspects of virus-host interactions, as well as reveal new cell biology principles.



Atan Gross

Biological Regulation

WHAT — Mitochondria Biology

HOW — Mitochondria in Health & Disease

MODEL ORGANISM — Mouse

MAJOR METHODS — Live-time imaging, Mitochondria Bioenergetics, Mouse genetics, Metabolomics, Proteomics

The major research topics of our lab evolve around how mitochondria act as “headquarters” to coordinate cell fate decisions and the relevance to disease.

KEYWORDS

- Mitochondria dynamics
- Metabolomics
- Apoptosis
- Mitochondria-nuclear communication

Dvir Gur

Molecular Genetics

WHAT Biological Crystallization Mechanisms

HOW We study the cellular processes used by organisms to produce optically functional or pathological bio-organic crystals

MODEL ORGANISM Zebrafish, Chameleons, Copepods, Medaka

MAJOR METHODS Light and Electron Microscopy, Spectroscopy, Molecular Biology, Single-cell RNA-seq, Gene editing

KEYWORDS

- Organic-biomineralizationn
- Biological photonics
- Pathological crystallization

Chameleons, copepods, fish, and many other organisms, use organic crystals for an astonishing variety of optical functions. These crystals are formed by specialized cells, in which remarkable control over crystal shape, size, and assembly is obtained using strategies that are beyond the state of the art in materials science. While these cells were identified many years ago, almost nothing is known about their biology, particularly the cellular processes involved in organic crystal formation. We use biological tools together with physical and chemical methodologies to study the processes organisms use to produce either optically functional or pathological, bio-organic crystals. Our main model organisms for these studies are zebrafish and medaka.

Jacob Y. Hanna

Molecular Genetics

KEYWORDS

- Stem cells
- Epigenetics
- Reprogramming
- Fertility
- Bioinformatics

WHAT Stem cell biology and epigenetics of early development

HOW We study the molecular foundations and applied potential of mammalian pluripotent stem cells in early development and in vitro

MODEL ORGANISM Mice, humans

MAJOR METHODS Tissue culture, gene editing, advanced microscopy, genomics, animal models

We are an interdisciplinary group of scientists interested in understanding embryonic stem cell biology, early development and advance human disease modeling. Specifically, we investigate the process of cellular reprogramming, in which induced pluripotent stem cells are generated from somatic cells, and we investigate how pluripotency is maintained throughout development in mouse and human. We utilize in our studies a diverse arsenal of biological experimentation methods, high throughput screening, advanced microscopy and genomic analyses. We also seek to combine biological experimentation with computational biology, theory and modeling, to elucidate the biological processes involved.

Eran Hornstein

Molecular Genetics

KEYWORDS

microRNA, ALS

Phase separation

Membraneless organelles

Mass-spectrometry

WHAT Non-coding neuro-genetics

HOW Omics molecular medicine approaches to RNA insufficiency in neurodegeneration

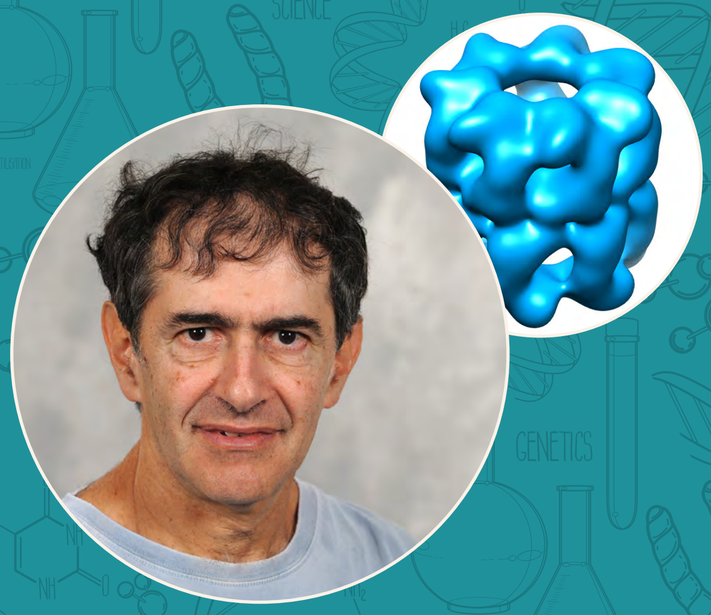
MODEL ORGANISM Human, mouse

MAJOR METHODS

- Proximity proteomics
- Human genetics
- Next generation sequencing

Hornstein lab investigates the molecular mechanisms underlying neurodegeneration. We are particularly interested in alterations in non-coding genetics and RNA metabolism of neurodegeneration. We study RNA-related neuro-protective functions and insufficiency in neuro-diseases, including amyotrophic lateral sclerosis (ALS) and FTD.

We use a multidisciplinary approaches, including computational data science, mouse genetics and iPS cell-derived human neurons. We also translate the molecular mechanisms we have discovered, that underlie neurodegeneration into potential therapies. We develop cell-free biomarkers and test a small molecule therapy based on our findings in a clinical trial.



Amnon Horovitz

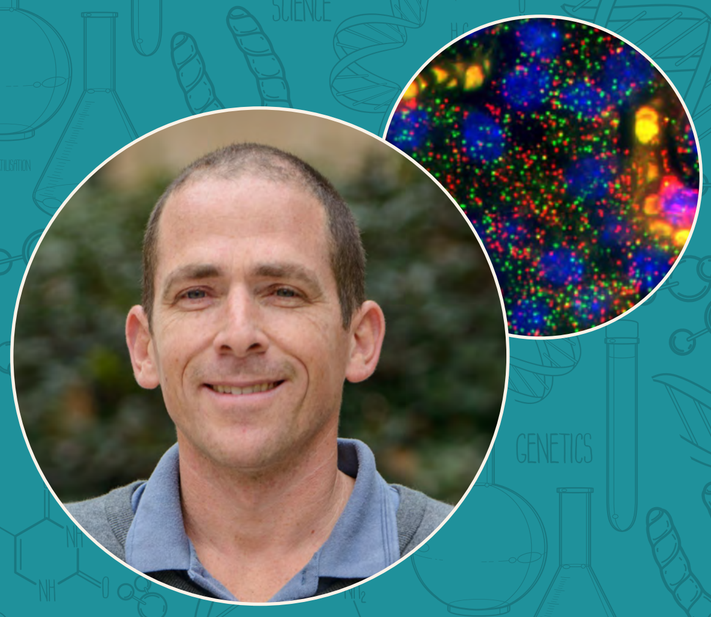
Structural Biology

KEYWORDS

- GroEL
- Chaperonins
- Allostery
- Protein folding
- Cooperativity

WHAT	Protein folding and allostery
HOW	Structure-function analysis of protein folding machines
MODEL ORGANISM	E. coli, yeast
MAJOR METHODS	Molecular biology, steady-state and transient kinetics, mass spectrometry

The focus of our research activities is to understand the molecular basis of allosteric transitions in protein machines and how they relate to their function. Much of our work is centered on the GroEL and CCT/TRiC folding machines in E. coli and yeast, respectively. We are interested in understanding their substrate specificity, folding mechanisms and allosteric properties.



Shalev Itzkovitz

Molecular Cell Biology

KEYWORDS

- Systems biology
- Division of labor
- Spatial transcriptomics
- Stem cells
- Metabolism

WHAT Systems Biology of mammalian tissues

HOW Single cell RNAseq and single molecule transcript imaging in intact tissues

MODEL ORGANISM Mouse, human

MAJOR METHODS

- Single cell RNAseq
- Single molecule transcript imaging
- Computational modeling
- FACS
- Mouse models

Mammalian tissues are composed of heterogeneous cells, interacting in highly structured microenvironments to achieve physiologic goals. We study how single-cell gene expression patterns serve to achieve these goals and how intercellular interactions are perturbed in disease such as diabetes and cancer. We apply an interdisciplinary approach, combining novel measurement techniques of single cells in intact tissues with mathematical models. We focus on the metabolic tissues – intestine liver and pancreas and apply cutting-edge technologies such as single cell RNAseq and single molecule microscopy.

Steffen Jung

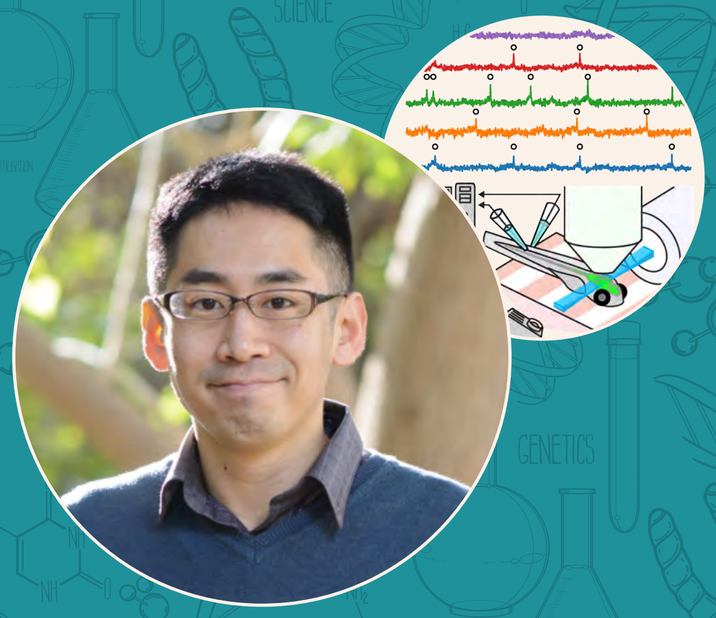
Immunology

KEYWORDS

- Macrophages
- Microglia
- IBD
- Inflammation

WHAT	Mononuclear Phagocyte Biology
HOW	We study in vivo functions of specific innate immune cells using state of the art mouse models
MODEL ORGANISM	Mouse
MAJOR METHODS	Flow cytometry, transcriptome and translatome profiling, conditional mutagenesis, advanced imaging

Mononuclear phagocytes form a body wide network of myeloid immune cells devoted to the maintenance of health and immune defense of the organism. We study these monocytes, dendritic cells and macrophages in physiological in vivo context, providing detailed mechanistic insights into intercellular communication driving human pathologies. Current focus is given to the gut and brain. Specifically, we investigate cytokine circuits that control the hyper-activation of macrophages in small and large intestine, as well as brain microglia, which otherwise leads to detrimental pathologies such as inflammatory bowel disorders (IBD), sickness behavior and neuropathy.



Takashi Kawashima

Neurobiology

KEYWORDS

Optical imaging

Statistics, serotonin

Genetics

WHAT Neuroscience

HOW Neural circuit mechanisms of adaptive behaviors, with a focus on the serotonin system

MODEL ORGANISM Zebrafish

MAJOR METHODS

- Large-scale recording of neural activity
- Statistical analyses
- Behavioral assays
- Genetic engineering

How does our brain mediate persistent behavioral changes? To answer this central question in neurobiology, we investigate how monoamine systems, such as the serotonin (5-HT) and dopamine (DA) systems, orchestrate whole-brain neural dynamics during adaptive and maladaptive behaviors.

We approach this problem using zebrafish, whose tiny transparent brain is an excellent model for the basic functionalities of our brain. We apply advanced optical imaging, statistical analyses and genetics to examine how whole-brain neural activity dynamics mediate behavioral changes and how monoamine systems modulate such dynamics.

Leeat Keren

Molecular Cell Biology

KEYWORDS

- Immunology
- Cancer
- Computational biology
- Multiplexed imaging
- Proteomics

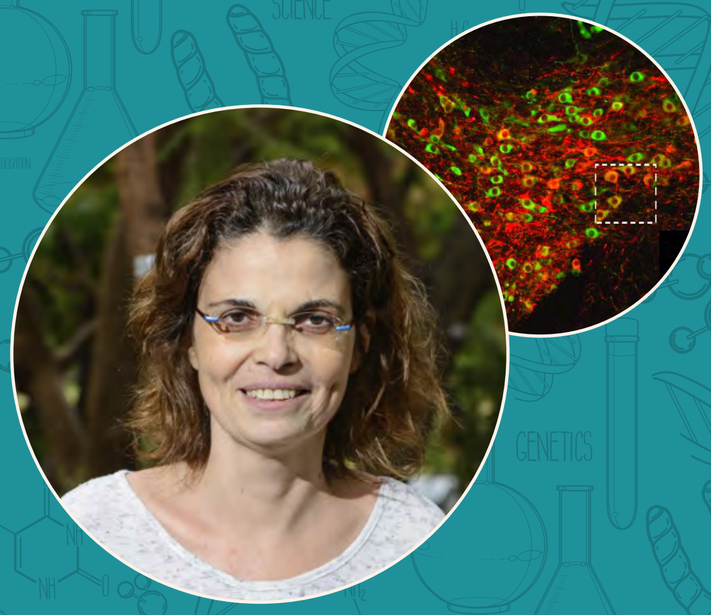
WHAT Systems pathology and immunology

HOW Developing experimental and computational approaches for multiplexed imaging of clinical specimens

MODEL ORGANISM Humans, Mice

MAJOR METHODS Multiplexed imaging , Computational biology , Mass cytometry , Machine learning , Histology

Human pathologies depend on the interplay between malignant cells, stroma, and the immune system. However, we have much better understanding of individual cells than of their cumulative behavior. Our research is focused on understanding how different cells interact as a system in health and disease to define progression and outcome in response to treatment. We develop new imaging tools to visualize the molecular composition of single cells in clinical specimens in unprecedented spatial detail. We combine these with artificial intelligence and clinical collaborations to study of trans-cellular interactions, with the ultimate goal of developing better treatments and diagnostics.



Tali Kimchi

Neurobiology

WHAT Behavioral Neuroscience

HOW Neurobiology of sexual dimorphism in social and reproductive behavior

MODEL ORGANISM Mice, Blind mole rat

MAJOR METHODS Behavior, Molecular biology, Neuronal manipulation, Neuronal tracing, Endocrinology

KEYWORDS

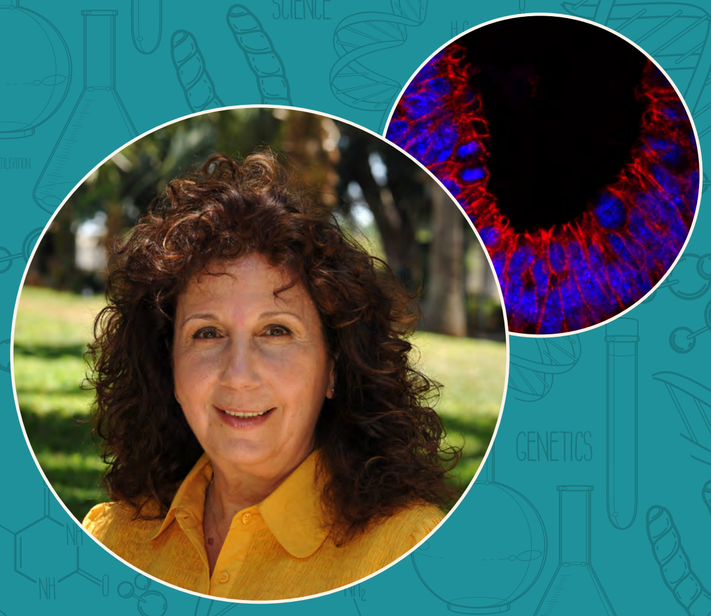
- Social behavior
- Sex difference
- Pheromone
- Neuronal circuit
- Hormones

We are studying the neuronal and molecular mechanisms that govern reproductive behavioral patterns and social interactions.

The lab focuses on two main themes:

1. 1. Elucidating how sexually dimorphic reproductive behaviors, such as mating, parental care and aggression, are encoded by the male and female brain, and regulated by environmental stimuli (focusing on olfactory signals).

2. 2. Dissecting the mechanisms underlying social behaviors and group organization in neurotypical and autism spectrum disorders (ASDs)-related mouse models



Adi Kimchi

Molecular Genetics

KEYWORDS

Cell death

Embryonic stem cell differentiation

Autophagy

Cancer therapy

Protein interaction networks

WHAT Cell death, autophagy, proteomic networks

HOW Molecular basis of life and death decision of a cell; implications in cancer and embryonic stem cell differentiation.

MODEL ORGANISM Human, mice

MAJOR METHODS

- Platforms monitoring protein-protein interactions
- RNA translation
- RIP assays- RNA immunoprecipitation
- Whole genome shRNA-mediated screens
- Immunostaining of cells and mouse embryos

Our lab studies programmed cell death, a network of multiple cell death and survival pathways, whose complex coordination determines a cell's decision to live or die. The following topics are being studied:

- Monitoring the global profile of protein- protein interactions of hundreds pairs of proteins, in cells in real time.
- Whole genome functional screens to identify drivers of alternative forms of programmed cell death.
- Mechanisms that suppress selective RNA translation to allow embryonal stem cell differentiation.
- Mechanisms of cell death in the developing mammalian embryo.
- Identifying the cell death signature of patient's tumors and targeting point of vulnerability towards precision cancer therapy.

Tamir Klein

Plant & Environmental Sciences

KEYWORDS

- Tree drought resistance
- Plant hydraulics
- Tree carbon relations
- Mycorrhiza
- Forest competition

WHAT

Tree Physiology and Forest Ecology

HOW

We study how water and carbon move inside trees, among trees, and between trees and their environment

MODEL ORGANISM

If you are a tree, we are coming for you

MAJOR METHODS

- Leaf gas exchange and stem sap flow
- Isotopic carbon composition
- Transcriptomic analysis
- Micro-CT
- Environmental monitoring

- We discover new insights into how trees cycle water and nutrients between leaves, stems, and roots—including a “carbon trade” between roots of nearby trees. We quantified the transfer of carbon between mature trees of different species in the forest.
- We investigate the drought-resistance mechanisms of trees. Even irrigation does not cancel out the exposure of fruit trees to drought, so the development of drought-resistant varieties of lemons, pears, and olives would allow them to grow in drier areas.
- Studying trees matters if we understand that they are an essential part of the global water and carbon budgets. In order to mimic what greenhouse gases might have in store for life on Earth 50 years from now, we adapted greenhouses with double the concentration of CO2 we have today.

Ilana Kolodkin-Gal

Molecular Genetics

KEYWORDS

- Biofilms
- Antibiotic resistance
- Host-microbe interactions
- Interspecies competition

WHAT	Molecular Microbiology and Microbial Communities
HOW	How do bacteria generate multicellular structures and acquire phenotypic antibiotic resistance?
MODEL ORGANISM	Bacillus subtilis; Pseudomonas aeruginosa
MAJOR METHODS	Fluorescent Microscopy; Electron Microscopy; Genetics; Transcriptomics

In nature, bacteria form complex and differentiated multicellular communities, known as biofilms. The coordinated actions of many cells, communicating and dividing labor, allow biofilms to attach to hosts and protect them from environmental assaults. Bacteria in a biofilm are up to 1,000 times more resistant to antibiotics than free-living bacteria. The mechanisms supporting this community resistance and the transition from free-living single bacteria to a differentiated biofilm colony are still poorly understood. We use single-cell imaging, genetics, transcriptomics, and biochemistry to identify novel bacterial developmental pathways. We study biofilm formation in beneficial bacteria as well as bacteria involved in persistent infections.

Valery Krizhanovsky

Molecular Cell Biology

KEYWORDS

- Aging, senescence
- senolytics
- cancer
- immune surveillance

WHAT Cellular Senescence

HOW We study why we age and how senescent cells impact aging, age-related diseases and cancer

MODEL ORGANISM Mice, Human

MAJOR METHODS Physiological analysis of mouse models, Flow cytometry, Gene editing, Gene expression analysis, imaging

Cellular senescence, a permanent cell-cycle arrest, limits tumorigenesis and tissue damage. However, the long-term presence of senescent cells can paradoxically promote tissue damage and aging. These non-cell-autonomous effects are partially mediated by the secretion of soluble factors from senescent cells to their microenvironment.

In order to understand the role of cellular senescence in cancer, aging and more recently in embryonic development, our research aims to uncover the underlying mechanisms associated with the interaction of senescent cells with their microenvironment.

We study how immune systems regulates the presence of senescent cells and thus age-related diseases.

Ilan Lampl

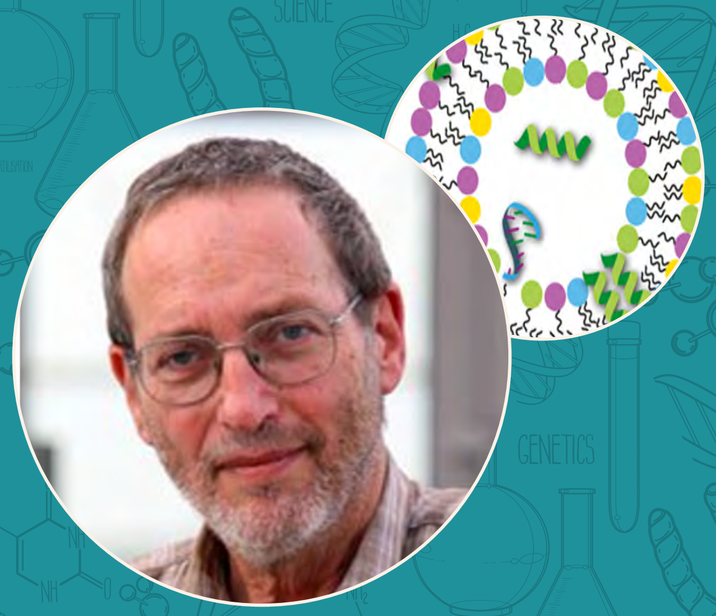
Neurobiology

KEYWORDS

- Cortical synchronization
- Sensory adaptation
- Balance excitation-inhibition
- Interhemispheric correlations
- Multimodal integration

WHAT	Sensory systems
HOW	Studying cellular correlates of tactile perception of rodents
MODEL ORGANISM	Mice
MAJOR METHODS	In-vivo intracellular recordings, multi-electrode arrays, 2 photon microcopy, optogenetics, head-fixed behaving mice

The neocortex plays a central role in higher brain functions, including perception, memory and motor control. Yet, basic anatomical and physiological features are similar across different cortical areas, suggesting that similar principles govern cortical functions. Our overarching research goal is to understand how tactile stimuli are represented by the somatosensory cortex and what enables their perception. Using in-vivo recordings, calcium imaging and optogenetics in awake mice, we study how neurons integrate excitatory and inhibitory inputs from local and distal sources and how their activity is affected by the history of stimulation as well as by the animal's behavioral state.



Doron Lancet

Molecular Genetics

KEYWORDS

- Catalytic networks
- Simplest reproduction
- Lipid World
- Evolutionary complexification
- Systems Prebiology

WHAT Prebiotic evolution

HOW Experimentally-rooted computational chemistry model for a lipid-centric early evolution of life

MODEL ORGANISM Protocells

MAJOR METHODS Systems Biology, Systems chemistry, Computational models, Kinetic simulations, Molecular Dynamics

We proposed a model for life's emergence, involving assemblies of lipids that, upon biased accretion and fission, pass compositional information to progeny. Our computational chemistry formalism (GARD) depicts non-equilibrium catalytic lipid networks with homeostatic growth, showing reproduction with mutations, hence capable of selection and evolution. Thus, RNA and proteins may be the outcome, not prerequisite for life's emergence. We now gather experimental evidence for catalysis in nanoscopic protocells, use Molecular Dynamics to support homeostatic growth, and employ advanced kinetics to show attractor behavior that could greatly enhance the probability of life in the universe.

Tsvee Lapidot

Immunology

KEYWORDS

- Stem Cells
- Neutrophils
- Melatonin
- Norepinephrine
- TNF

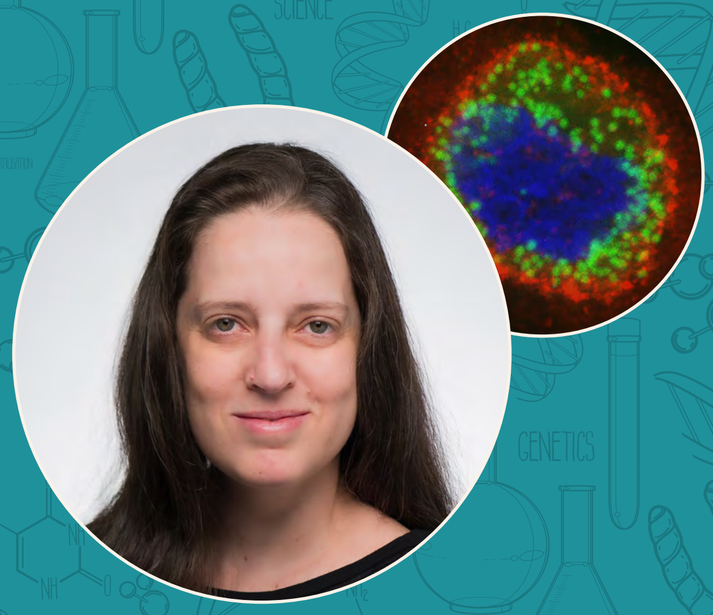
WHAT Regulation of the bone marrow reservoir of immature leukocytes

HOW Regulation of host immunity by the bone marrow microenvironment

MODEL ORGANISM Functional preclinical mouse models (also for human hematopoietic stem cells)

MAJOR METHODS Bone marrow stem cell transplantation. LPS induced gram negative bacterial infections. Light and darkness onset mediated immune cell generation and replenishment of the bone marrow reservoir

Metabolic regulation of hematopoietic stem cell migration and development by their dynamic bone marrow (BM) microenvironment and BM neutrophil activation and recruitment. The role of daily circadian light and darkness onset, ROS, nitric oxide, lactate, mitochondria transfer, the endothelial BM/Blood barrier, TNF, Norepinephrine, Melatonin, CXCL12/CXCR4 interactions, proinflammatory Thrombin/PAR1 interactions, anti-inflammatory aPC/EPCR/PAR1 stem cell regulation, clinical stem cell mobilization, homing and repopulation are currently investigated.



Orly Laufman

Molecular Genetics

✉

KEYWORDS

- RNA viruses
- Infectious disease
- Virus-host interactions
- Organelles

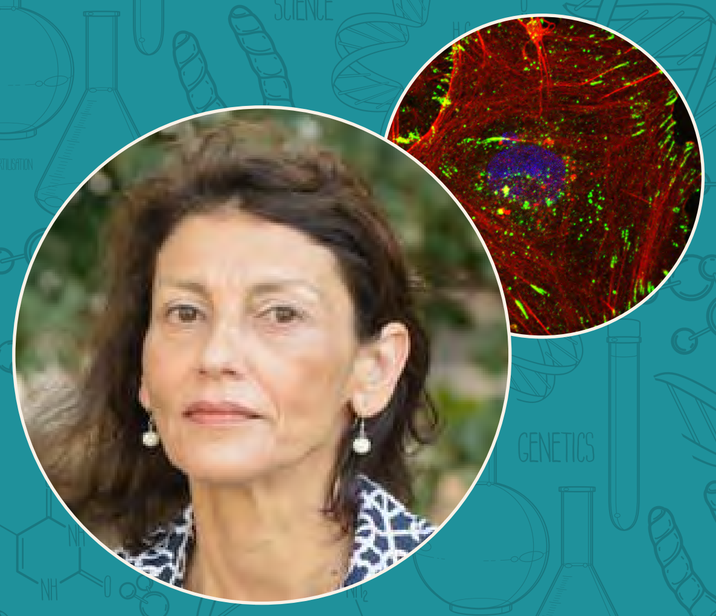
WHAT Molecular and cell biology of RNA viruses

HOW We study how RNA viruses transform their host cells into viral manufactories

MODEL SYSTEM Enteroviruses

MAJOR METHODS Microscopy, molecular biology, protein-protein interaction analysis, genetic manipulations, virus assays

RNA viruses including corona, zika and dengue are a major threat to human health. We study how RNA viruses interact with their host cells and transform them into viral manufactories. Our main model is enteroviruses (EVs), common human pathogens, that cause severe medical complications in young children. We tackle key questions including: How EVs that express only a handful of proteins take control over human cells with complex protein machineries? How EVs hijack host organelles and repurpose them into a makeshift virus factory? We aim to build a complete mechanistic picture of the EV replication process, that will help develop better antivirals, for a broad spectrum of RNA viruses.



Sima Lev

Department of Molecular Cell Biology

KEYWORDS

- Signaling networks
- Intracellular trafficking
- Targeted therapy
- Drug resistance
- TNBC

WHAT Cancer cell biology

HOW Signaling networks in cancer development and metastasis

MODEL ORGANISM Human & mice

MAJOR METHODS
Human and mouse cell culture (2D & 3D)
Mouse cancer models
Cell signaling & membrane trafficking-associated methods
Confocal microscopy
Bioinformatics

Aberrant signaling networks commonly lead to uncontrolled cell growth, proliferation and motility, and consequently to cancer development and metastasis. We aim to identify tumorigenic alterations in signaling networks and target them for cancer therapy. We focus on triple negative breast cancer (TNBC), a highly aggressive subclass of breast cancer. We apply multidisciplinary approaches to gain molecular understanding of how TNBC develops, progresses and spreads to eventually identify highly effective therapeutic strategies for each individual patient.

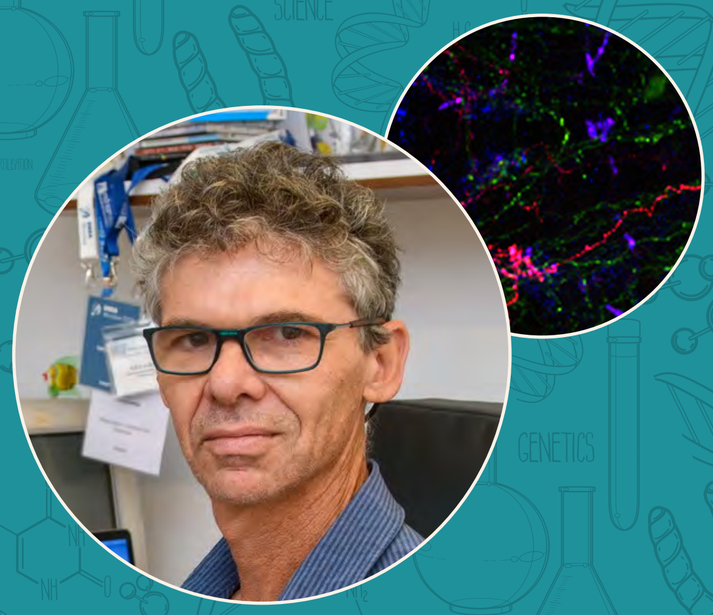
Ongoing projects focus on:

(1) Ferroptosis

(2) Tumorigenic signaling networks

(3) EMT and drug resistance

(4) Synthetic lethal interactions.



Gil Levkowitz

Molecular Cell Biology

WHAT

Development and function of the hypothalamus

HOW

We study morphogenesis, cell biology and function of hypothalamic neurons, which regulate appetite, stress and social behavior

MODEL ORGANISM

Zebrafish

MAJOR METHODS

Genome editing, transgenesis, imaging, behavioural analyses, cell biology

KEYWORDS

- Oxytocin
- Neuro-vascular
- Stress
- Social behavior
- Neurohypophysis

We utilizes zebrafish to investigate development and function of neurons that reside in the hypothalamus. These neurons regulate fundamental body functions including sleep, blood pressure, temperature, hunger and metabolism, thirst and satiety, stress and social behavior. We study the molecular and cellular processes underlying morphogenesis and function of oxytocinergic neurons that affect both peripheral and central nervous system activities. A primary research direction is the assembly and maintenance of the hypothalamo-neurohypophyseal system. This important neuroendocrine conduit between brain and blood contains multiple neurovascular interfaces that mediate the passage of hormones to the peripheral blood circulation.

Emmanuel Levy

Structural Biology

KEYWORDS

- Protein interactions
- Networks
- Structure
- Proteomes

WHAT Structural Systems Biology

HOW A quantitative and structural understanding of cells and their proteome

MODEL ORGANISM S. cerevisiae, H.sapiens

MAJOR METHODS Computational Biology, Robotics, Microscopy, Yeast genetics, Modeling

Our understanding of biology has been revolutionized by the development of genomic and proteomic technologies, in particular with deep sequencing and mass spectrometry. Such technologies have been providing precise information about parts (DNA, RNA, proteins) that make up a cell. Remarkably, however, our understanding of how these parts self-organize and give rise to a living cell have been lagging behind. The overarching goal of our research is to characterize general principles by which proteins self-organize in space and time. In this endeavor, we develop computational as well as experimental approaches and bridge different fields of biology.

Koby Levy

Structural Biology

WHAT Computational Molecular Biophysics

HOW Dynamics and mechanism of proteins and DNA self-assembly

MODEL ORGANISM Any

MAJOR METHODS Computational biology, Molecular dynamics simulations, simplified models, bioinformatics

KEYWORDS

- Transcription
- Molecular transport
- Protein folding
- Modelling

We focus on deciphering the mechanisms and kinetics of various biomolecular self-assembly processes. Quantifying the molecular and physical principles of the mechanisms of protein-protein and protein-DNA assembly is key to cracking the protein-DNA recognition code and improving the prediction of specificity and binding affinity.

Our goals are to predict new phenomena and principles from the physical and chemical perspective as well as providing molecular interpretation to basic cellular processes, for understanding diseases and ways to overcome them.

Zvi Livneh

Biomolecular Sciences

KEYWORDS

- DNA repair
- DNA damage
- Mutagenesis
- Cancer prevention
- Cancer early detection

WHAT DNA repair – mechanisms and utility in fighting cancer

HOW Molecular analysis using human cultured cells and cooperation with hospitals in clinical experiments

MODEL ORGANISM Homo Sapiens

MAJOR METHODS Molecular Biology; CRISPR; Unique DNA repair assays; DNA sequencing; Embryonic stem cells

We study the molecular mechanisms by which DNA damage, caused by internal and external agents, is handled by human cells, including embryonic stem cells. We focus on the balance between error-free and error-prone mechanisms, and in particular the role of low-fidelity DNA polymerases, which we discovered, and which are a major source of mutations. In parallel we develop blood tests to measure DNA repair, and use them in clinical and epidemiological studies for prevention and early detection of cancer. Notably, we discovered that a DNA repair score combined of 3 DNA repair blood tests, is a strong risk factor for lung cancer, and can be utilized for prevention and early detection.

Yoav Livneh

Neurobiology

WHAT Neuroscience of brain-body communication

HOW Combining systems neuroscience, behavior, and bodily physiology

MODEL ORGANISM Mouse

MAJOR METHODS Two-photon imaging, optogenetics, behavior, peripheral physiological measurements and manipulations

KEYWORDS

- Insular cortex
- Interoception
- Motivation
- Hunger
- Thirst

Brain-body communication requires interoception, the perception of internal bodily signals. Insular cortex is the main cortical site that integrates external cues with bodily signals. We seek to understand brain-body communication, and its role in regulating diverse behaviors, by focusing on insular within the brain-body loop. We focus on global physiological need states such as hunger and thirst, as well as on more specific signals such as gut nutrient sensing. We use cellular/sub-cellular imaging, with circuit-mapping, circuit manipulation and computational approaches. We combine these approaches with goal-directed behaviors, as well as measurements and manipulations of bodily physiology.

Nir London

Organic Chemistry

KEYWORDS

- Covalent
- Drug discovery
- Cancer
- Chemical probes
- Docking

WHAT Chemical Biology

HOW We use computers, chemistry and biology to design covalent ligands for interesting targets

MODEL ORGANISM Proteins

MAJOR METHODS Virtual screening, Empirical screening, Medicinal Chemistry, Mass spectrometry, Cell culture work

Covalent inhibitors have many advantages as chemical probes and drug candidates, discovery of new covalent inhibitors remains challenging, however. Our lab is interested in covalent molecular recognition, the development of technologies to design and discover such covalent inhibitors and their application to shed new light on biology. We have developed two leading technologies for covalent probe discovery. The first is DOCKovalent, a software that computationally screens huge libraries of putative covalent binders. The second is a complementary, empirical, electrophile fragment-based approach. Through both, we were able to rapidly discover covalent fragment hits for several protein targets. We now develop additional approaches related to targeted protein degradation, proteomic target identification and new screening modalities.

Ron Milo

Plant & Environmental Sciences

KEYWORDS

- Lab evolution
- Synthetic biology
- Quantitative biology
- Anthropocene
- Climate change

WHAT The interface of systems biology with sustainability

HOW Our group brings the tools of systems biology to bear on the grand challenges of sustainability.

MODEL ORGANISM E. coli

MAJOR METHODS Thinking, talking, evolving, multiplying, hiking

My lab members and I are passionate about trying to understand the cellular highways of energy and carbon transformations known as central carbon metabolism in quantitative terms. We employ a combination of computational and experimental synthetic biology tools. We also quantify the new geological era of the anthropocene from a holistic quantitative perspective to get insight and lead of action.

Filipe Natalio

Kimmel Center for Archaeological Science and Plant & Environmental Sciences

KEYWORDS

- material farming
- biological fabrication
- cotton
- hominins's behavior
- artificial intelligence

WHAT

Material farming and archaeological/ anthropological science

HOW

Merging plant with material sciences (material farming). Artificial Intelligence algorithms applied to archaeology and anthropology

MODEL ORGANISM

Cotton (Gossypium hirsutum), hominins

MAJOR METHODS

Single Cell Transcriptomics, Enzymology, Protein Expression, Hybrid Synthetic Biology-Chemistry, Electron Microscopy, Raman Spectroscopy, AI algorithms

Our lab focuses on two different research areas: archaeology/anthropology and material farming. On the archaeology/anthropology, we are developing AI algorithms (in 2D and 3D) to infer past human behavior. On the material farming, we are combining the study of cotton natural biochemical pathways at different scales and hybrid synthetic biology-chemistry to exogenously "bioaugment" cotton fibers with unusual properties (e.g. fluorescence, hydrophobicity or magnetism).

Michal Neeman

Biological Regulation

WHAT	Imaging of angiogenesis
HOW	Multi modal molecular imaging of regulatory checkpoints in vascular remodeling
MODEL ORGANISM	Human, mouse, cell culture
MAJOR METHODS	MRI; 2 photon microscopy; MSOT; CT; light sheet microscopy

KEYWORDS

Angiogenesis

lymphangiogenesis

reproduction

placenta

cancer

The vascular bed is essential for survival of all multicellular organisms larger than a millimeter. Accordingly, structural and functional changes of tissues, in health and disease, during development or degeneration, are accompanied and often induced by vascular changes.

The aim of our work is to map the regulatory network controlling the growth and function of blood and lymphatic vessels. Novel MRI tools, accompanied by advanced optical modalities, allow us to non-invasively obtain dynamic information on activity of multiple steps in the angiogenic process and thereby improves our understanding of the key regulatory elements and critical checkpoints of vascular remodeling.

Moshe Oren

Molecular Cell Biology

WHAT	Cancer Biology
HOW	Tumor suppression by p53 and the Hippo pathway
MODEL ORGANISM	Mouse (and humans)
MAJOR METHODS	fluorescent imaging, bulk and single cell RNA-sequencing, global-“omic” analyses, in vivo mouse tumor models and gene manipulation by CRISPR-Cas9 and other methods

KEYWORDS

- tumor suppression
- cancer-associated mutations
- molecular signaling
- transcription
- tumor microenvironment

The p53 tumor suppressor gene is the most frequently mutated gene in human cancer. When functional, p53 drives a transcriptional program leading to elimination of cancerous cells. In contrast, cancer-associated p53 mutations not only abolish its anti-tumor activity, but also facilitate tumor progression through pro-oncogenic gain of function. Current research in our lab focuses on the involvement of wild type tumor suppressive p53 and mutant oncogenic p53 in transcriptional regulation, metabolism, shaping the tumor microenvironment and anti-cancer immunity.

We are also interested in the Hippo pathway, which is emerging as a master controller of tumor growth and metastasis.

Meital Oren-Suissa

Neurobiology

WHAT Molecular Neurobiology

HOW The synaptic basis for sexual dimorphism in the nervous system

MODEL ORGANISM *C. elegans, mouse, cell culture*

MAJOR METHODS Transsynaptic labeling, single-cell RNA-seq, optogenetics, calcium imaging and genetic analysis.

KEYWORDS

- Sex-specific connectivity
- Neuronal circuits
- Sensory function
- Dimorphic behaviors
- Connectomics

Sexual dimorphisms in brain structure and function are evident across phylogeny, but little is known about sexually dimorphic features of individual neurons, and the mechanisms for establishment and maintenance of dimorphic neuronal circuits. The Oren lab investigates how sexually dimorphic patterns in the brain emerge, from synapse formation to animal behavior. We have developed a unique system that enables studies of sexual dimorphism at the synaptic, circuit, genetic and behavioral levels, across all developmental stages. We are also testing how sexual dimorphism is manifested in brain pathologies.

Rony Paz

Neurobiology

KEYWORDS

- Electrophysiology
- fMRI
- Computational neuroscience
- Learning
- Memory

WHAT Systems Neuroscience and Brain Research

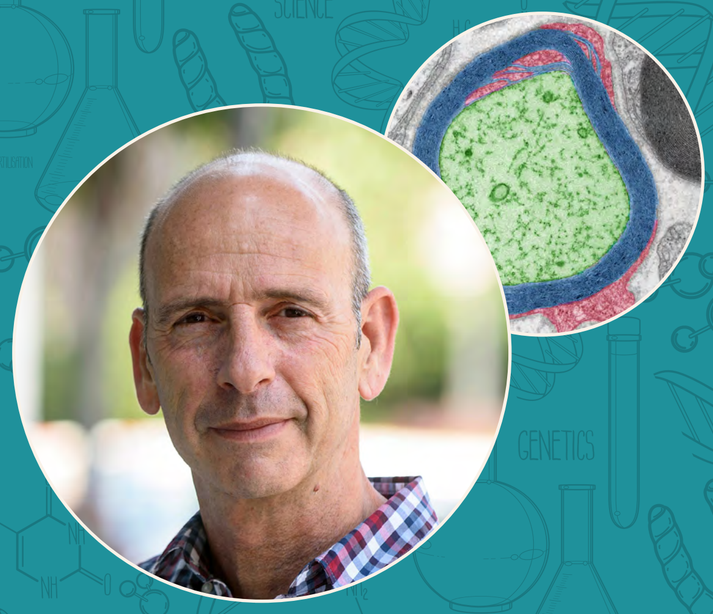
HOW Neural networks mechanisms that underlie learning and memory, and related models of neuropsychiatry

MODEL ORGANISM Humans; non-human-primates

MAJOR METHODS Electrophysiology; fMRI; brain-stimulation; computational approaches to analyses of neural data

How can 10^11 neurons, each forming 10^4 connections with other neurons, work in concert to process information and underlie cognitive functions? What is the neural language/code? We focus on dynamics of networks during learning and memory formation. We combine electrophysiology in animals, fMRI in humans, and computational methods, to unveil mechanisms that underlie learning and memory formation.

We investigate phenomena as: reinforcement learning, generalization of learning, emotional modulation, extinction of memories, primitives of computation, social cognition. We develop models for pathologies that arise from abnormalities in learning and memory, as PTSD, Depression, Anxiety and Autism.



Elior Peles

Molecular Cell Biology

KEYWORDS

- Myelin
- Axon
- Schwann cells
- Oligodendrocytes
- Axon-glia interaction

WHAT

Cellular and Molecular Neurobiology - Myelin Biology

HOW

Combine molecular, biochemical and advanced microscopy techniques to study myelinating glial cells

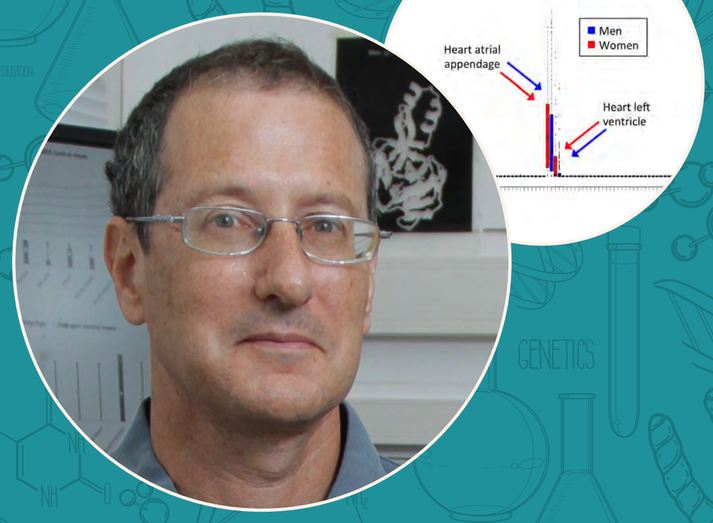
MODEL ORGANISM

Mouse

MAJOR METHODS

- Primary neuronal and glial cultures
- Fluorescence and electron microscopy
- Molecular proteomics
- CRISPR-based genome modification

Myelin is an insulating membrane sheath produces by specialized glial cells; Schwann cells in the peripheral nervous system (PNS) and oligodendrocytes in the central nervous system (CNS). It enables fast and efficient nerve conduction, and provides essential trophic support to maintain axonal integrity and survival. Destruction of myelin leads to several neurological diseases such as multiple sclerosis, and is also associated with psychiatric and neurodegenerative disorders. We study the various aspects of myelinating glial cells biology, and in particular interested in the mechanisms that enable Schwann cells and oligodendrocytes to ensheath the axons they contact and to myelinate them.



Shmuel Pietrokovski

Molecular Genetics

KEYWORDS

Gene-expression programs

Human tissues transcriptomes

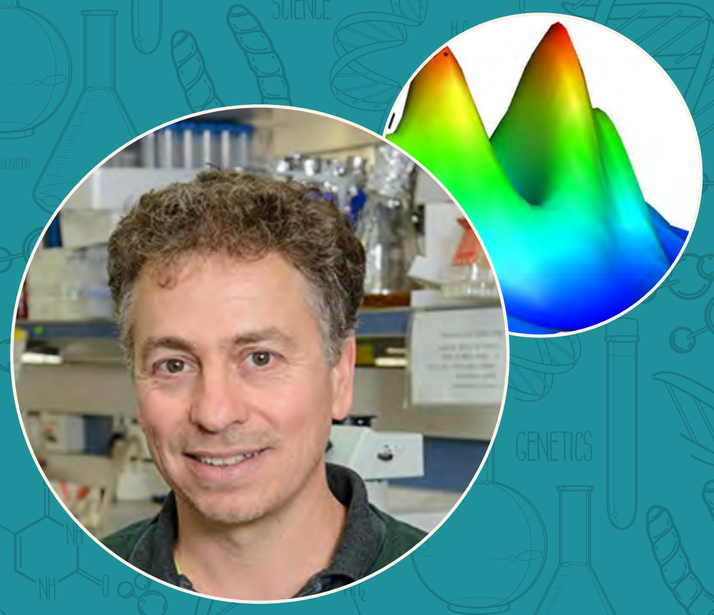
WHAT Computational biology

HOW Large-scale analyses of human-individuals expression data - What is 'normal'?

MODEL ORGANISM Human

MAJOR METHODS Computer programing; Statistics

High quality RNAseq data of 53 tissue types is available for >700 individuals. We are interested in examining unusual expression programs. Besides typical ‘normal’ expression of each gene in each tissue are fewer cases where individuals have much higher or lower expression values for some genes in some tissues. These cases might be due to individuals in atypical conditions that led to atypical expression. Identifying these individuals and genes requires analyses across all individuals, tissues, and genes. Finding the common pathway/s of these genes might determine what was the atypical condition that led to their unusual expression.



Yitzhak T. Pilpel

Molecular Genetics

KEYWORDS

- Evolution
- Regulation
- Translation
- Bioinformatics

WHAT Genomics, Systems Biology, Evolution

HOW We study the structure, function and evolution of systems that regulate gene expression, with emphasis on translation

MODEL ORGANISM Yeast, E. coli, human

MAJOR METHODS Experimental evolution, computational biology and modeling, synthetic biology

We study the structure, function and evolution of genetic regulatory networks in microbes and mammals. We use computational biology and theory to formulate hypotheses on evolution of regulatory networks. A main research paradigm is experimental evolution with which we evolve organisms in the lab to tackle basic questions on dynamics and mechanisms of evolution. We aim to distil genetic determinants of evolvability – the capacity of organisms to evolve. We use lab evolution to reveal the role of evolutionary mechanisms such as horizontal gene transfer, and reverse transcription. A major focus is on regulation of protein translation in which we study efficiency and fidelity of the process.

Michal Ramot

Neurobiology

KEYWORDS

Cognition

Function

Integration

Behavior

WHAT	Networks, behavior and plasticity in the human brain
HOW	Large scale interactions at the network level, and their relationship to behavior
MODEL ORGANISM	Humans
MAJOR METHODS	fMRI, electrophysiology, computational approaches, neurofeedback

Integration is the hallmark of cognition. This is true both at the neural, and at the behavioral level. Even the single action potential is above all the product of large-scale integration across multiple brain regions. The simplest, everyday behaviors (for instance remembering a face, or opening a door) are in actuality incredibly complex, supported by multiple cognitive domains such as perception, action, memory, learning, and social cognition. Our group studies those large-scale interactions, and how they support the network level synthesis of interdependent cognitive processes in health and disease.

Neta Regev-Rudzki

Biomolecular Sciences

WHAT Infectious Disease, Microbiology, Malaria

HOW Studying cell-cell communication mechanisms of malaria parasites within a population and with their hosts

MODEL ORGANISM *Malaria parasite, Plasmodium falciparum*

MAJOR METHODS Molecular Biology, Microscopy, Microbiology, Biophysics and Immunology

KEYWORDS

- Parasitology
- Extracellular vesicles
- Cell-communication
- Pathogen-host interaction
- Infectious diseasev
- Microbiology

AT THE MOLECUAR FRONTIERS OF CELL-CELL COMMUNICATION IN PARASITOLOGY.

Malaria, caused by Plasmodium falciparum, is the most devastating parasitic disease, killing up to a half a million people each year. We have previously showed that malaria parasites can communicate between them using secreted Extracellular Vesicles (EVs). EVs capable of delivering cargo of proteins, lipids and nucleic acids by fusing with target distal cells, thus providing a secure and efficient mode for signal delivery. Little is currently known about the precise mechanisms of parasite-derived EV cargo delivery and function. With malaria continuing to be a major global disease, advances toward understanding the basic biology of Plasmodium remain essential.

Ziv Reich

Biomolecular Sciences

KEYWORDS

- Directed evolution
- Population dynamics
- Photosynthesis
- Crop engineering
- Structural biology

WHAT

Biophysics, Photosynthetic machineries, crop engineering, population diversity and dynamics

HOW

Our studies proceed along two major lines: (I) Structural, functional and ontogenic aspects of photosynthesis and engineering of drought-resistant nutritious plants and (II) The relationship between individuals, communities, environment and time

MODEL ORGANISM

S. Cerevisiae, Craterostigma pumilum

MAJOR METHODS

Multi-omics, microfluidics, microscopy, electron-tomography, crispr technologies, modelling

We study:

- Structure, function & adaptability of photosynthetic machineries.
- Biogenesis and breakdown of the photosynthetic apparatus during leaf development and senescence.
- Structural, molecular and regulatory mechanisms of desiccation tolerance in resurrection plants.
- Engineering out toxins from drought-tolerant nutritious plants for human consumption.
- What is the relationship between environmental dynamics and population variability and survivability?
- To what extent is the ability of individuals to survive deterministic/stochastic?
- Can individuals, or communities as a whole, acquire new adaptive functions following training by synthetic feedbacks?

Orly Reiner

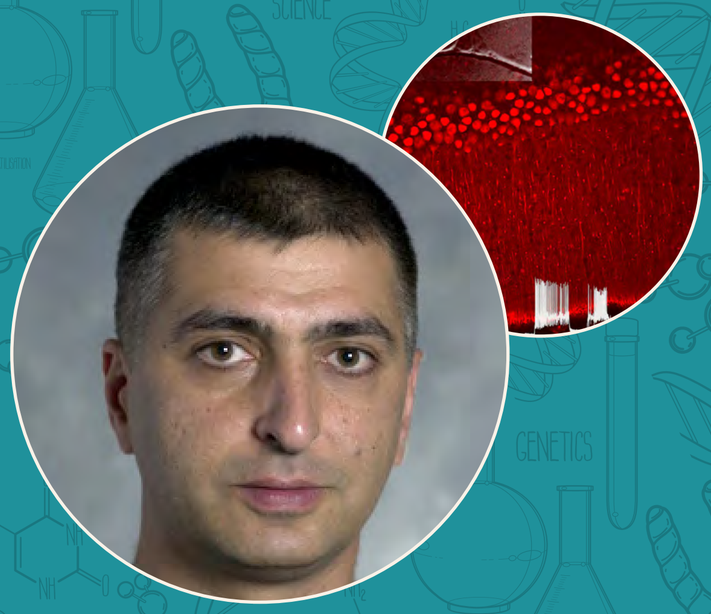
Molecular Genetics

KEYWORDS

- Microcephaly
- Lissencephaly
- Autism spectrum disorder
- Epilepsy
- Schizophrenia

WHAT	Brain development in Health and Disease
HOW	Elucidating pathways involved in brain development and what goes wrong in case of developmental brain diseases
MODEL ORGANISM	Human, Mouse
MAJOR METHODS	Human brain organoids, CRISPR/Cas9, mouse genetic models, in utero electroporation

We study the process of embryonic brain development, and what goes awry during disease conditions. In the developing brain there is a relative change in the type of neuronal stem cells that are born; and neurons born in one position have to reach their final destination by active cell migration. These highly dynamic processes are regulated via the concerted action of multiple gene products. Through interdisciplinary approaches, combining molecular, biochemical, in vivo, ex vivo, and in vitro studies with mouse and human brain organoid models, we examine a wide range of human developmental brain malformations and diseases.



Eitan Reuveny

Biomolecular Sciences

KEYWORDS

- Ion channels
- G protein coupled receptors
- Imaging
- Calcium

WHAT

How neurons and cells regulate their electrical activities and calcium levels, from molecular insights to behavior

HOW

We are interested in deciphering questions spanning from molecular to behavioral levels

MODEL ORGANISM

Mice; Xenopus Laevis (forgs, as source for oocytes for heterologous expression). Cultured cells and neurons

MAJOR METHODS

Electrophysiology, Two photon imaging (also in vivo), animal behavior, standard molecular and protein expression techniques, molecular dynamics simulations

Ion flow through protein channels is one of the fundamental mechanisms of transmembrane signaling. Ion channels are involved in processes as diverse as development, hormone secretion, salt balance and memory. Abnormalities in channel function underlie a wide range of neural, muscular, cardiovascular and renal diseases. In order to understand the roles of ion channels under normal and pathological conditions, it is necessary to know how they regulate the flow of specific ions across the membrane and how other proteins affect their function. We address these questions by combining state of the art electrophysiological, molecular and imaging techniques, both in cultured cells and in native tissues.

Michal Rivlin

Neurobiology

KEYWORDS

- Retina
- Neural circuits
- Neuronal plasticity
- Synaptic mechanisms
- Visual pathway

WHAT Neural circuits in the visual system

HOW Functional imaging and electrophysiology to uncover light responses of neurons along the visual pathway and their underlying circuits

MODEL ORGANISM Mouse

MAJOR METHODS Two-photon calcium imaging, patch-clamp techniques, multi-electrode array recordings, computational modeling, immunohistochemistry

The retina is a model system in neuroscience. It is easily accessible and its input can be fully controlled by the investigator. Its simple layered structure combined with the recent advances in microscopy, imaging and genetics place the retina in a unique position to study computations in neuronal circuits.

Recently, we found that retinal neurons can dynamically change their computation (=the visual property they report on). We study the mechanisms allowing anatomically-defined neural circuits to change their function, and investigate how retinal targets decode the dynamic signal.

We also aim to use the retina for early diagnostic of neurodegenerative diseases, such as Parkinson's disease.

Rina Rosenzweig

Structural Biology

KEYWORDS

- Molecular chaperones
- Protein folding
- Protein aggregates & amyloid fibers
- Magnetic resonance
- Biochemistry

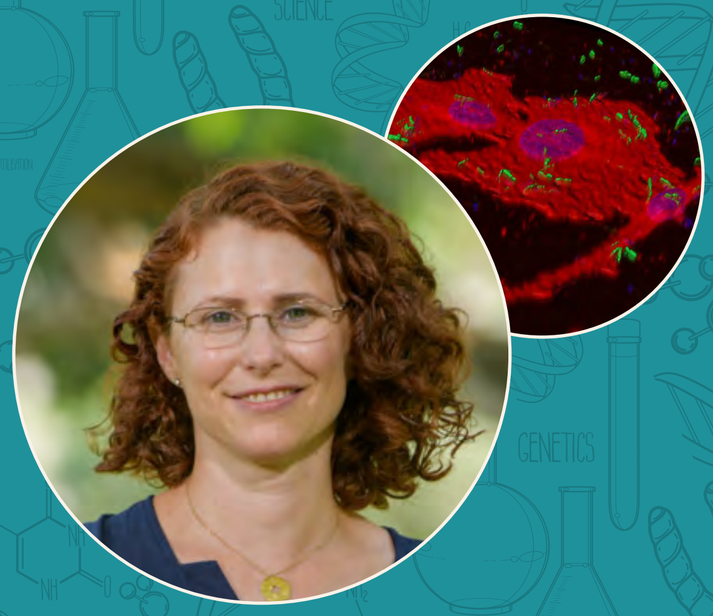
WHAT Structure and function of human molecular chaperones

HOW Combining biochemical and biophysical assays with cutting edge magnetic resonance techniques

MODEL ORGANISM Human proteins

MAJOR METHODS Magnetic resonance (NMR), biochemistry, biophysics, electron microscopy

Our lab studies molecular machines in our cells, called chaperones, that can reverse the formation of toxic protein aggregates and amyloid fibers linked to a host of debilitating conditions, such as ALS, and Parkinson’s, Alzheimer's, and Huntington's diseases. We use a combination of advanced NMR (magnetic resonance) techniques and biochemical and biophysical functional assays to obtain a structural and mechanistic understanding of how these chaperones work, and the conformational changes they impose upon their clients to do so. Through this research we aim to identify why, in certain cases, chaperones fail in their task - giving rise to disease.



Yardena Samuels

Molecular Cell Biology

KEYWORDS

- Melanoma
- Neo-peptides
- Immune-response
- Checkpoint inhibitors
- Somatic mutation

WHAT

Cancer immune-genomics

HOW

An integrative approach for the exploration of melanoma genetic and immunological interactions

MODEL ORGANISM

Human and mouse models

MAJOR METHODS

- Next generation sequencing and analysis
- HLA peptidomics
- T cell receptor sequencing
- Cytof
- Mouse models

Our aim is to delineate the interactions of melanoma cells with the immune system. To this end we have established an extensive melanoma genetic database and a pipeline to identify and characterize neoantigens using whole-exome and HLA peptidomics in order to further understand its functional implications. This allowed us to map both the neoantigenic and T cell receptor landscape, their immune reactivity and corresponding T cell identities. We have further established a powerful melanoma mouse model that allows us to identify novel clinically-relevant biomarkers and treatment options for melanoma patients.

Rita Schmidt

Neurobiology

KEYWORDS

Ultra-high field MRI

High resolution imaging

WHAT

Imaging the human brain: ultra-high field MRI and new biomarkers

HOW

Developing new tools for human MRI, especially at ultra-high field 7T MRI scanner, aiming to better understand the human brain function

MODEL ORGANISM

Humans

MAJOR METHODS

- Targeting high resolution imaging to separate layers and columns in the brain structure
- Advancing dedicated MR pulse sequences to achieve fast and ultrafast high quality MR imaging and spectroscopic imaging
- Exploring new methods for mapping electric properties of the tissues as a new contrast for structural and functional brain MRI
- Grasping the correlation between the MR electrical properties and the possible contributors to the functional process
- Boosting the accessible MR signal in localized functional brain trials

The study of MRI and of functional MRI is a prime example of contemporary multidisciplinary science; where Physics, Chemistry, Biology and Engineering meet. In our lab we integrate these fields aiming to develop new imaging methods and new tools for functional brain measurements. The study relies on the one hand on a physics background, for the development of new MRI techniques, on the other hand on a neurobiology background, to perform the actual human volunteer studies. Our lab's research focuses on ultra-high field MRI aiming to better understand the human brain function. To do so, we are looking for new biomarkers and contrast methods, as well as new methods of acquisition.

Gideon Schreiber

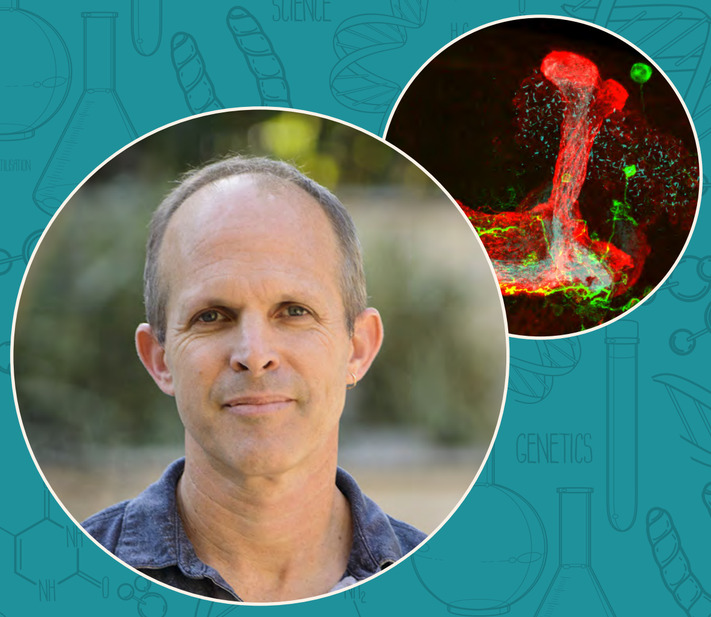
Biomolecular Sciences

KEYWORDS

- In vitro evolution
- Protein-protein interactions
- Covid-19
- Interferon
- Signaling

WHAT	Biochemistry
HOW	From protein-protein interactions to biological regulation
MODEL ORGANISM	Human, E.coli, Yeast
MAJOR METHODS	In vitro evolution, biophysical methods, molecular biology

Specific protein-protein interactions are basic in all living processes. My laboratory studies structure/function relations of protein-protein interactions and how these relate to biological signaling. For this purpose, we adopted a multidisciplinary approach including biophysical and biological bench work, protein- engineering, bioinformatics and applied the gained knowledge towards solving biological questions. Recently, we started to work on the evolution of the SARS-CoV-2 virus, showing that its in vitro evolution parrots and predicts contagious mutation spread. Moreover, we successfully evolved a drug, that is now in animal experiments. Other research topics include the evolution of specificity of protein-protein interactions and the molecular understanding of the type I interferon system.



Oren Schuldiner

Molecular Cell Biology

KEYWORDS

- Neuronal remodeling
- Pruning
- Neuronal degeneration
- Axon regeneration
- Circuit formation

WHAT Developmental Neuroscience

HOW Mechanisms of axon growth, destruction and refinement during developmental neuronal remodeling

MODEL ORGANISM Fruit Fly *(Drosophila melanogaster)*

MAJOR METHODS

- Genetics
- Confocal Imaging
- Mosaic analysis
- RNAseq
- Connectomics

Our lab is interested in neuronal remodeling, which is critical for setting up the wiring diagram of the nervous system. When defective, it is implicated in a wide range of neuro-psychiatric disorders including autism, schizophrenia and Alzheimer's. Remodeling involves both degeneration and regeneration. Therefore, our studies have the potential to shed light on axon degeneration and regeneration during development, in disease and following injury.

Maya Schuldiner

Molecular Genetics

KEYWORDS

- Mitochondria
- Peroxisomes
- Endoplasmic Reticulum
- Protein-targeting
- Contact-sites

WHAT Organelle Biology

HOW Functional genomics and systematic screens to uncover new protein functions

MODEL ORGANISM Baker's yeast *(Saccharomyces cerevisiae)*

MAJOR METHODS High content screens, gene editing, gene knock-out, protein tagging, spinning disk microscopy

A hallmark of eukaryotic cells is the presence of membrane-enclosed organelles that create optimized environments for chemical reactions required to sustain life. Although more than 20 years have passed since publication of the yeast genome sequence, over 30% of organelle proteins have never been studied and more than half do not have a known function. Most of these proteins are conserved all the way to humans and some have been implicated in diseases. We use novel methodologies to uncover the functions of these unstudied proteins, and to delineate pathways and networks that enable the function and communication of organelles.

Michal Schwartz

Neurobiology

WHAT Neuroimmunology

HOW The role of immune system in brain homeostasis and repair: implications to aging and Alzheimer's disease

MODEL ORGANISM Rodents

MAJOR METHODS Animal behavior, cognitive tests, immunogenomics, biochemistry, flowcytometry, CyTOF

KEYWORDS

- Neuroinflammation
- Immunotherapy
- Microglia
- Alzheimer's disease
- Dementia

Schwartz's laboratory focuses on the role of innate and adaptive immunity in brain plasticity in health and disease. The team discovered: 1. The pivotal role of the systemic immune system in brain plasticity and repair (Nature Medicine, 1998; Nature Medicine. 1999; PLOS Medicine, 2009; Nature Neuroscience, 2006); 2. The brain's choroid plexus epithelium, as a physiologically active immunological interface between the brain and the immune system, and as an entry gate for leukocytes, needed for brain homeostasis and repair (Immunity, 2013; Brain 2013); 3. Dysfunction of this interface in aging and neurodegenerative diseases (Science, 2014; J. Neuroscience, 2015; Nature communication, 2015), and that unleashing the immune system (Immunotherapy) can combat Alzheimer's disease (Nature Communications, 2015; Nature Medicine, 2016; Science, 2017; J. Ex. Med, 2018; Nature Communications, 2019).

Schraga Schwartz

Molecular Genetics

KEYWORDS

- Regulation of gene expression
- RNA modifications
- Computational biology

WHAT	The epitranscriptome
HOW	The through which diverse post-transcriptional modifications regulate the fate of mRNA
MODEL ORGANISM	Yeast and mammalian cell lines
MAJOR METHODS	Genomics; Genetics; Computational biology; System biology; Molecular Biology

RNA is modified by >100 chemical modifications. These modifications are, in some cases, highly ubiquitous, conserved and dynamically regulated in mRNA, imposing a unique and uncharacterized regulatory code. Our lab aims to crack this code, and understand how modifications on mRNA direct gene expression programs and cell state decisions. Our lab bridges experimental and computational aspects of biological research, combining genomic, genetic and biochemical approaches with tailored computational ones.

Eran Segal

Computer Science &
Molecular Cell Biology

KEYWORDS

- Computational biology
- Microbiome
- Personalized medicine

WHAT	Personalized Medicine
HOW	Personalized medicine using machine learning applied to genomic and clinical data
MODEL ORGANISM	Human
MAJOR METHODS	Machine learning and big data analysis

We are a multi-disciplinary lab of computational biologists and scientists focusing on microbiome, nutrition, genetics, and gene regulation in health and disease. We aim to develop personalized nutrition and personalized medicine using machine learning, computational biology, probabilistic modeling, and analysis of heterogeneous genomic and clinical data.

Einat Segev

Plant & Environmental Sciences

KEYWORDS

- Microbial interaction
- Marine microorganisms
- Chemical ecology
- Biogeochemistry

WHAT Marine Microbiology, Biogeochemistry

HOW We study microbial interactions in the ocean, combining microbiology, ecology and geochemistry

MODEL ORGANISM We study an algal-bacterial model system containing the alga *Emiliania huxleyi* and the bacterium *Phaeobacter inhibens*

MAJOR METHODS Fluorescent Microscopy, genetic manipulation, organic and inorganic compound analyses, metagenomics and transcriptomics, field studies

Microscopic algae that live in the ocean are fundamental in the global carbon, oxygen and sulfur cycles. In recent years we have begun to learn that microalgae associate with marine bacteria in exquisite ways; the whole range from mutualism to pathogenicity can be seen in algal-bacterial interactions. Our group studies how algae and bacteria communicate via organic and inorganic compounds. Through a unique combination of approaches from the Life and Earth sciences, we aim to understand how algae and bacteria influence each other, the marine environment, and the geological record of Earth.

Idit Shachar

Immunology

KEYWORDS

Cancer

Autoimmunity

B cells

Immunotherapy

Stem cells

WHAT

Immunotherapy of cancer and autoimmunity by regulating the immune cells' survival and function

HOW

Decipher expression of molecular pathways and their function in cells, disease models and samples from patients.

MODEL ORGANISM

Mouse models and Human patient samples

MAJOR METHODS

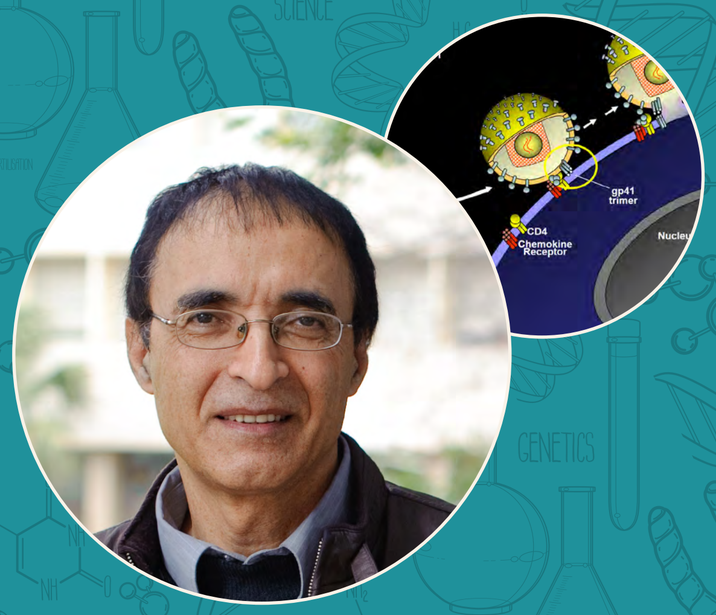
- Flow Cytometry
- In vivo disease models (Cancer and Autoimmune disease)
- In Vitro culture manipulations
- Genomic and bioinformatics research

Adaptive immunity depends on generation and maintenance of a pool of mature peripheral lymphocytes throughout life. Lymphoid homeostasis results from delicately balanced lymphocyte production, differentiation, sequestration, proliferation, and survival. Disturbing this balance can lead to autoimmune malfunctions such as autoimmune diseases and cancer evasion of the immune system.

Our studies focus on four main aspects of the regulation of immune cell maintenance:

1. Regulation of stem cell maintenance
2. Molecular pathways controlling immune cell survival in homeostasis and malignancies
3. Cross-talk of immune cell with their microenvironment
4. Control of regulatory B cells differentiation and function in autoimmune diseases and cancer
5. Regulation of anti-tumor immunity in hematological and solid tumors.

Finding of our studies can pave the way towards development of novel therapies for various malignancies and autoimmune diseases.



Yechiel Shai

Bimolecular Sciences

KEYWORDS

HIV

Biofilm

Cystic fibrosis

Innate immunity

Protein-protein interactions

WHAT

Peptide-membrane interactions and peptide-protein recognition in diseases

HOW

Peptide chemistry, molecular genetics, biochemistry, biophysics, in-vitro and in-vivo studies

MODEL ORGANISM

Human (Homo sapiens), Mouse (Mus musculus), Pseudomonas aeruginosa, Salmonella Typhimurium

MAJOR METHODS

- Peptide synthesis
- HPLC (High-Performance Liquid Chromatography)
- Biophysics and biochemistry methods (FRET, CD, FTIR, Fluorescence Microscopy Western-blot)
- Tissue culture and microbiology (Isolation of primary cells/tissue, bacterial assays) Molecular biology (Cloning, RT-PCR, ELISA, proliferation assays, RT-PCR)

1. Antimicrobial peptides (AMPs) are innate immunity molecules in all life forms. We study their mode of action which allow us to design AMPs with high potency against planktonic bacteria and biofilms. Moreover, we study resistance mechanisms towards AMPs.

2. HIV is a viral pathogen which infects the host via the gp41 protein. We study the mechanism by which HIV infects its target cells and escape the immune response.

3. TLRs sense pathogens and initiate the immune response. Uncontrolled activation of TLRs might lead to pathologies ranging from cystic fibrosis, Crohn's disease and cancer.

Importantly, these studied lead also to the design of peptides which block various steps in the function of the protein and hence can be developed to novel therapeutics to various diseases.

Michal Sharon

Biomolecular Sciences

KEYWORDS

- Mass spectrometry
- Protein degradation
- Regulatory mechanisms
- Protein complexes
- Structure-function relationship

WHAT Structural Mass Spectrometry

HOW We combine native mass spectrometry analysis with biochemistry and cell biology

MODEL ORGANISM Human, mice, rat, yeast, bacteria

MAJOR METHODS Native mass spectrometry, Cell biology, Biochemical assays, FACS, Microscopy

We aim to discover the mechanisms that control and coordinate the activity of molecular machines involved in the protein degradation pathway. To do so we apply novel native mass spectrometry approaches, in conjunction with fluorescence microscopy, biochemical and cell biology methods - generating an integrative mode of analysis combining in vitro and in vivo findings.

Efrat Shema

Biological Regulation

KEYWORDS

Chromatin

Epigenetics

Cancer

Single-Molecule

WHAT Cancer Epigenetics

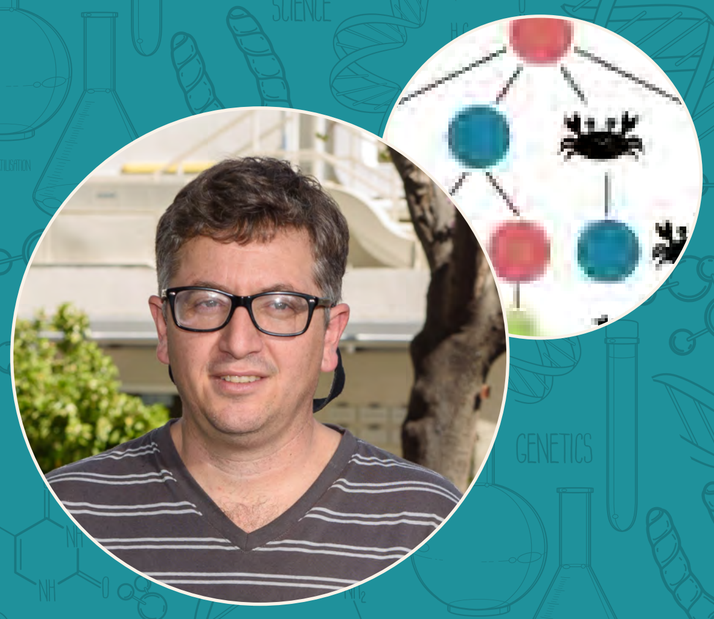
HOW We study epigenetic events that contribute to cancer by applying innovative single-molecule technologies.

MODEL ORGANISM Human

MAJOR METHODS

- Single-molecule imaging
- RNA-seq
- ChIP-seq
- CyTOF
- Super-resolution imaging

We study epigenetic events that contribute to cellular transformation and cancer. To address these fundamental questions, we develop and apply innovative cutting-edge single-molecule technologies. The activity of genes, and thus the establishment and maintenance of a cell's identity, is regulated by their cell type-specific chromatin organization. We develop methodologies at the interface of genomics and proteomics, with the goal of paving the way towards deeper understanding of epigenetic regulation, as well as the development of therapeutic and diagnostic tools. We focus on pediatric brain cancers, breast cancer and lymphoma.



Liran Shlush

Immunology

KEYWORDS

- HSCs
- Aging
- Bone marrow microenvironment
- Preleukemia

WHAT

Aging of the blood system and leukemia

HOW

Why the human hematopoietic system is aging and how it relates to the evolution of leukemia. Can we diagnose leukemia early and apply preventive therapy. Why mutations accumulate in HSCs and how do they change their function

MODEL ORGANISM

Human, Mice

MAJOR METHODS

Deep error corrected DNA NGS, single cell RNA and DNA sequencing, whole genome sequencing, RNA sequencing, CHIP & ATACseq

The aging of the human hematopoietic system is typically correlated with: 1) clonal hematopoiesis 2) myeloid malignancies 3) reduced T and B cell clonal diversity 4) reduced myeloid cells function 5) red to yellow marrow transition. Understanding the evolutionary principals driving these phenotypes is the first step in early diagnosis and treatment of hematopoiesis malfunction. Hematopoiesis failure in humans is a long process of somatic selection. Somatic evolution creates new clones exploring the fitness space. Without changes in the somatic environment new clones will loose to the young hematopoietic system which have been optimized over millions of years of germline evolution. Under changing environment, the fittest clones will gradually take over and in time due to antagonistic pleiotropy will lead to a disease. Our lab is a multidisciplinary lab composed of hematologists, evolutionary biologists and computationalsystem biologists all trying to understand the rules of human hematopoietic aging.

Ofer Shoshani

Biomolecular Sciences

KEYWORDS

- Chromosome biology
- Cancer evolution
- Drug resistance
- ecDNA
- DNA repair

WHAT Chromosome Catastrophes in Cancer

HOW Manipulating chromosomes to study the mechanisms and consequences of chromosome instability

MODEL ORGANISM Human (cell lines and patient samples), Mouse (cell lines and mouse models)

MAJOR METHODS Live cell imaging; cytogenetics; Genome editing; Whole genome sequencing; Single cell genomics

Chromosome abnormalities play an important role in cancer. Recent DNA sequencing efforts revealed the extent of cancer genome complexities. Our work identified how such abnormalities can drive cancer, and lead to therapy resistance.

We aim to uncover molecular mechanisms leading to catastrophic genomic events by developing chromosome manipulation approaches. This will help better understanding cancer evolution and drug resistance formation. Ultimately, we aim to identify vulnerabilities of cancer cells, specifically related to the role of DNA repair in initiating and maintaining chromosome abnormalities, with the intention of developing novel therapies that would prevent resistance formation.

Ruth S. Shouval

Biomolecular Sciences

KEYWORDS

- Tumor microenvironment
- Sstress responses
- Cancer
- Tumor heterogeneity

WHAT Cancer research

HOW We study the tumor microenvironment, and how it is transcriptionally rewired by stress to promote cancer

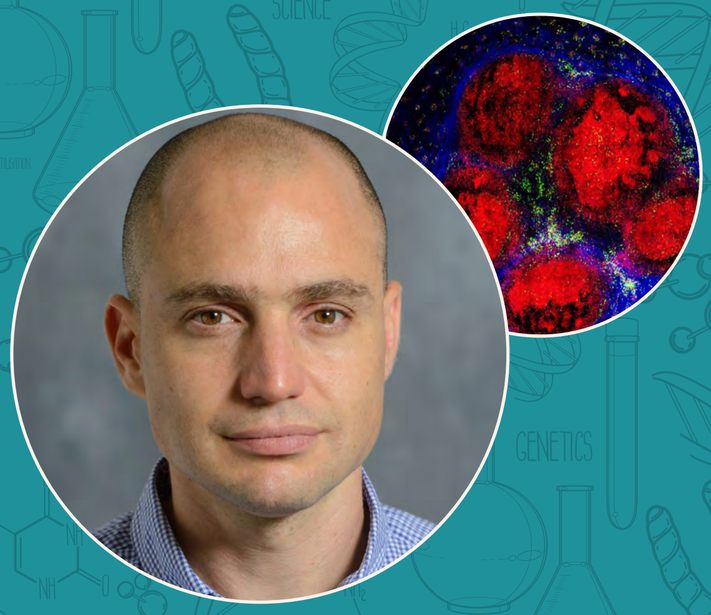
MODEL ORGANISM Mouse models, patient samples, cell culture

MAJOR METHODS RNA-sequencing, rPCR, Immunofluorescence, mouse genetics, cell culture

For tumors to expand, metastasize, and evade immune surveillance, cancer cells must recruit non-malignant cells, including macrophages, fibroblasts and endothelial cells. These cells, collectively termed the tumor microenvironment, are reprogrammed to support the tumor at the expense of its host.

We hypothesize that this reprogramming is mediated by evolutionary conserved stress responses, and we aim to elucidate these underlying mechanisms.

Our goal is to understand how tumors develop into systemic malignancies, predict which tumors are more likely to do so, and design therapeutic strategies to overcome these malignancies by targeting genetically stable elements in the tumor microenvironment.



Ziv Shulman

Immunology

KEYWORDS

Immunotherapy

Immunology

Antibodies

Lymphocytes

WHAT

Protective immune responses and antibody discovery

HOW

We study how antibodies are generated in response to invading pathogens in mouse models, infected subjects and cancer patients. We use this information to produce novel antibodies for immunotherapy.

MODEL ORGANISM

- Human tissues
- Transgenic mice

MAJOR METHODS

- Antibody cloning
- High throughput sequencing techniques
- Intravital imaging

Long lasting protection from harmful pathogens depends on collaboration of multiple types of immune cells each with a unique function. These cells interact with each other in small confined niches in lymphoid organs and exchange mo lecular signals required for differentiation into cells with the capacity to eliminate invading pathogens. Protective antibodies evolve in lymphoid organs in sites known as germinal centers. In our lab we aim to understand this process and discover new antibodies and targets for cancer immunotherapy and for treatment of various infectious diseases.

Yoav Soen

Biomolecular Sciences

KEYWORDS

Lamarckian adaptation

Novel challenge

Epigenesis

Host-microbiome interactions

Real-time learning

WHAT How Individual-specific adaptation comes about?

HOW Investigating how adaptation arises at the individual (as opposed to a population) level

MODEL ORGANISM

MAJOR METHODS

- Experimental analysis of how individual flies cope with severe challenges prior to selection of adaptive responses to the challenge
- Analysis of epigenetic, symbiotic and metabolic changes in response to stressful conditions that mimic a novel challenge
- Testing the predictions of a theory of individual-specific adaptation
- Theoretical models of individual-specific adaptation and its connections with learning without a guiding algorithm
- Specific methods include genomics, metabolomics and microbiology

Our group investigates how every cell and animal copes with stress that cannot be effectively alleviated by pre-existing adaptation, whether new adaptations can be acquired by semi-stochastic changes in the epigenome and microbiome, how these changes might affect the germline and how they can be inherited and stabilized as longer-term, evolutionary adaptations. Our focus is on testing predictions of a theory of individual-specific adaptation, which complements natural selection by explaining adaptation on every timescale and level of organization. It also explains induction of adaptive variations (a neglected gap in Darwin's theory) and accounts for the frequently invoked, but never really explained notion of adaptive plasticity.

Rotem Sorek

Molecular Genetics

KEYWORDS

CRISPR

Phage

Bacteria

WHAT Microbial genomics and systems biology

HOW We study the interactions between bacteria and the viruses that infect them

MODEL ORGANISM Bacteria

MAJOR METHODS Genomics, genetics, microbiology

We study how phages attack bacteria, and how bacteria defend themselves against such attacks.
We are interested in deciphering the molecular mechanisms providing bacteria with protection against phages, collectively known as the "immune system" of bacteria. Specifically, we study the CRISPR-Cas system, which is the adaptive immunity system of microbes, as well as new anti-phage defense systems discovered in our lab.
We also discovered that phages can use small-molecule communication in order to coordinate their infection dynamics - our lab studies the molecular mechanisms allowing such communication.

Ivo Spiegel

Neurobiology

KEYWORDS

- Experience-dependent plasticity
- Transcriptional network
- Cortical circuits
- Cell-type-specificity
- Synapses

WHAT	Molecular Systems Neuroscience
HOW	Genomic regulation of neural circuit plasticity
MODEL ORGANISM	Mouse
MAJOR METHODS	Genomics, molecular biology, viral tracing, electrophysiology, in vivo calcium imaging

Our ability to adapt to and learn from experiences underlies many of our cognitive capabilities. We seek to identify the molecular mechanisms through which neural circuits adapt to experience and to understand how the cellular functions that are regulated by these molecular mechanisms generate an animal's adaptive behavior. We focus in our research on signaling and transcriptional networks and apply genomic, molecular, biochemical, electrophysiological and in vivo imaging approaches to understand how experience-induced signaling and transcriptional networks in subtypes of cortical neurons regulate the connectivity and function of the cortex. We believe that our research will allow us to untangle how nature and nurture cooperate to regulate adaptive behavior and to understand how mutations in the genome might give rise to individual variation in cognitive capabilities and to psychiatric disorders.

Yonatan Stelzer

Molecular Cell Biology

KEYWORDS

- Epigenetics
- DNA methylation
- Embryonic Development
- Germ Cells and Reprograming
- Parental Imprinting

WHAT	Epigenetics
HOW	We study the functional roles of epigenetics during cell-fate decisions
MODEL ORGANISM	Mouse
MAJOR METHODS	Embryonic Stem Cells, Genome and Epigenome Editing, Single-Cell Genomics, Mouse Genetics and Transgenic, Microscopy

Epigenetic modifications provide cells and organisms with remarkable plasticity. Yet, disentangling the Gordian knot of epigenetic cause and effect still remains a formidable task. Building on the recent developments in single cell genomics and epigenomics and moving forward, by developing systems for dissection of embryonic epigenetic function in-vivo, represents a deep and fundamental challenge our group is determined to engage. Specifically, we ask:

- How cell-specific epigenetic programs are established and maintained?
- How do epigenetic changes at regulatory regions modulate cell state and function?
- What are the effects of epimutations on development and disease?

Ravid Straussman

Molecular Cell Biology

KEYWORDS

- Tumor microbiome
- Tumor microenvironment
- Cancer Immunotherapy
- Drug resistance
- Translational personalized medicine

WHAT

Tumor microenvironment, tumor microbiome and resistance to anti-cancer therapy

HOW

We try to advance precision anti-cancer therapy by better understanding of the tumor complexity

MODEL ORGANISM

Human, mouse, 3D tissues, cell lines

MAJOR METHODS

Next-generation sequencing (bulk/ single cell), High-throughput screening, Microscopy, ex-vivo organ cultures, Molecular & computational biology

Tumors are heterogeneous and are made of highly complex ecosystems. Accordingly, our studies reach beyond the tumor cells to include the multiple components of the tumor microenvironment, including stromal cells, immune cells and bacteria that are present inside tumors - the tumor microbiome. We use cutting edge technologies to characterize understudied components of the tumor microenvironment and the mechanisms that modulate the response to cytotoxic, targeted and immune-mediated anti-cancer therapies. We strive to develop better treatment options for cancer patients.

Dan Tawfik

Biomolecular Sciences

KEYWORDS

- Enzyme
- Evolution
- Origin of life
- Xenobiotics
- Decontamination

WHAT Enzyme structure, function and evolution

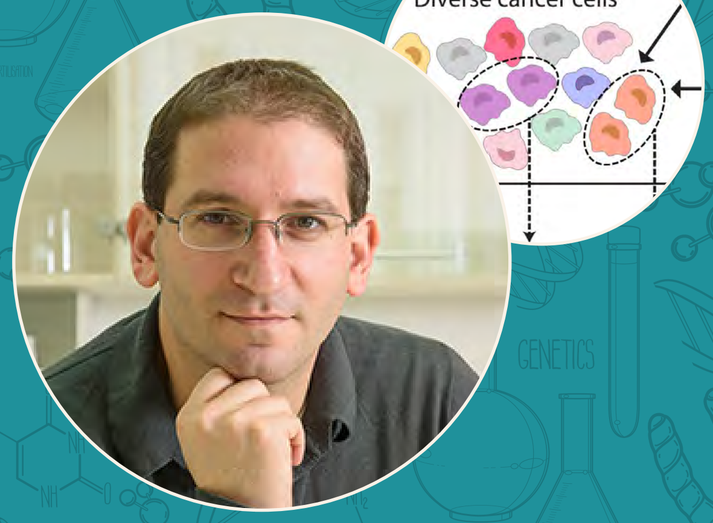
HOW We reconstruct the birth of new enzymes in the laboratory

MODEL ORGANISM Per project

MAJOR METHODS Bioinformatics, molecular biology, biochemical and biophysical methos

From the earliest proteins to modern synthetic biology and chemical biology, understanding evolution at the molecular level is fundamental to biology.

How do proteins evolve? Natural selection can create molecular machines with breath-taking performances, e.g., enzymes that accelerate the rate of chemical transformations by factors of 106 up to 1017. Strikingly, new protein functions can evolve within years or even months, as happens with drug resistance, and with enzymes that degrade man-made chemicals. Why is this process, which is based on ‘trial and error’ so rapid and efficient? We lack the fossils of the protein world, but we can reproduce protein evolution in the laboratory and in real time, implementing the principles of Darwinian evolution to individual genes and enzymes. In doing so, we obtain crucial insights regarding the evolutionary intermediates and the routes and mechanisms that led to the highly proficient enzymes known to us today.



Itay Tirosh

Molecular Cell Biology

KEYWORDS

- Tumor heterogeneity
- Glioma
- Single cells
- Systems biology

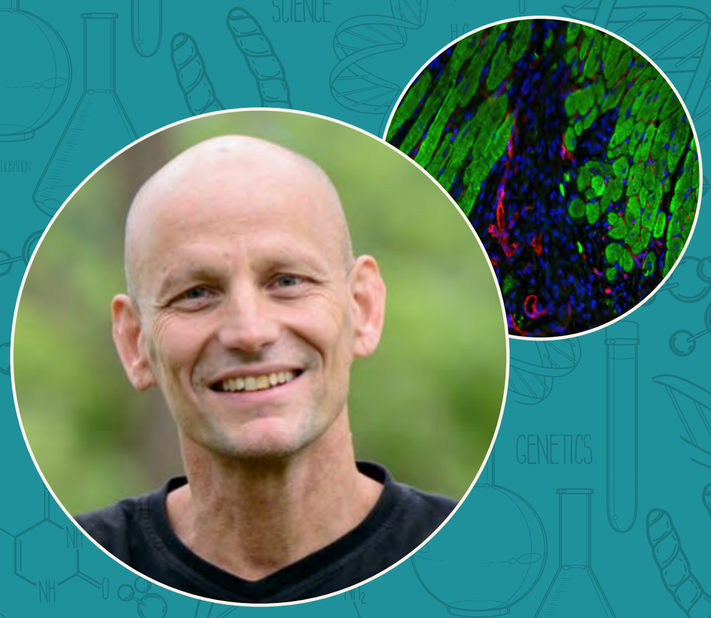
WHAT Cancer Biology

HOW Single cell genomics and computational approaches

MODEL ORGANISM Clinical tumor samples and cell-culture models

MAJOR METHODS Single cell RNA-seq, data analysis

We leverage single cell technologies, computational approaches and clinical collaborations to study human tumors as a complex ecosystem in which diverse cancer and non-cancer cells interact and collectively determine tumor biology and response to therapies. We analyze the diversity of cells within human tumors, to identify important tumor subpopulations such as cancer stem cells, drug resistant cells and invasive cells. We then study their function, regulation and vulnerabilities, with the ultimate goal of developing better cancer treatments.



Eldad Tzahor

Molecular Cell Biology

KEYWORDS

- Cardiac regeneration
- Regenerative biology
- Translational research
- Molecular signaling
- Awesome work!

WHAT	Regenerative biology
HOW	How to mend a broken heart?
MODEL ORGANISM	House mouse (Mus musculus)
MAJOR METHODS	Surgical myocardial infarction (heart attack), Echocardiography (ultrasound), Immunofluorescence, Western blot, Fluorescent activated cell sorting (FACS)

Ischemic heart disease is the leading cause of death in the Western world. We combine novel approaches to study and manipulate various aspects of cardiac physiology including cardiac muscle cells dedifferentiation and renewal, immune modulation and formation of new blood vessels to promote cardiac regeneration following injury. Aspiring towards the development of translational therapies , we have recently began work on a clinically relevant pig model of acute myocardial infarction (heart attack), to mimic the human setting as close as possible.

Our unique approach is to combine developmental biology and regenerative medicine aiming to develop novel therapies for mammalian heart regeneration.

Nachum Ulanovsky

Neurobiology

KEYWORDS

- Hippocampus
- Place cells
- Navigation
- Social neuroscience
- Natural behaviors

WHAT Behavioral and Systems Neuroscience

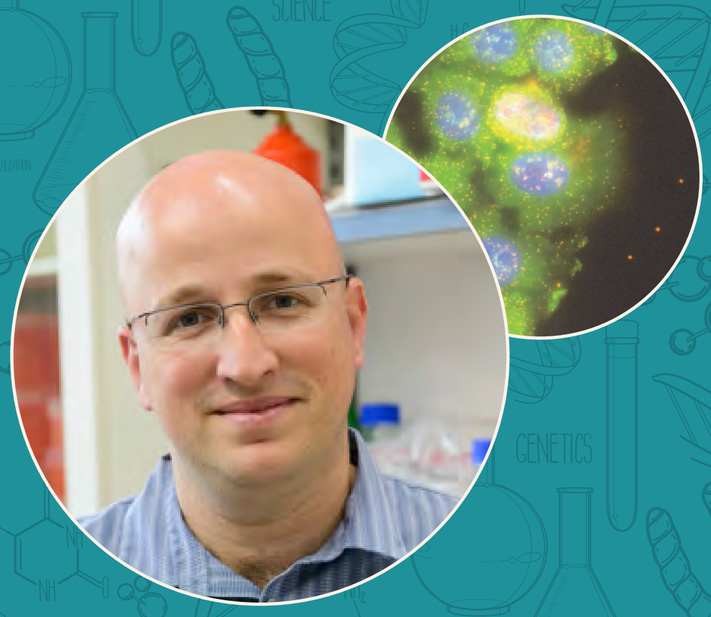
HOW Neural mechanisms of navigation, spatial cognition and social cognition in the hippocampus

MODEL ORGANISM Bats

MAJOR METHODS

- Wireless Electrophysiology in-flight
- 3D behavioral tracking
- On-board audio recordings
- Computational analyses

We take a “Natural Neuroscience” approach, which aims to decipher the neural mechanisms of natural behaviors in freely-moving animals. We focus on studies of neural codes for space, time, and social behaviors – in flying bats – using wireless electrophysiology methods that we pioneered. We discovered novel neuronal representations in animals navigating in 3D or in huge environments (hundreds of meters), or engaged in social interactions. These include 3D place cells and 3D grid cells, as well as “vector cells” representing the direction and distance to goals, and “social place-cells” representing other animals. Going forward, we want to take brain research to evermore naturalistic behaviors.



Igor Ulitsky

Biological Regulation

KEYWORDS

- Long noncoding RNAs
- Nuclear export
- Chromatin remodeling
- Bioinformatics
- High-throughput screens

WHAT RNA biology

HOW Characterization of the functions and mechanisms of long noncoding RNAs and of nuclear RNA export

MODEL ORGANISM Human and mouse cell lines, mouse models

MAJOR METHODS RNA-seq, computational biology, CRISPR, FISH, ChIP-seq

The human genome produces tens of thousands of long noncoding RNAs (lncRNAs), which are molecularly similar to mRNAs, yet do not encode functional proteins. lncRNA expression varies across tissues and is commonly dysregulated in human disease, including cancer. Accumulating evidence shows that lncRNAs play pivotal regulatory roles in diverse biological processes. Our goal is to understand how these functions are carried out and how they are encoded in lncRNAs sequences and structures. We are also interested in how the post-transcriptional fate, including nuclear export, of mRNAs and lncRNA is controlled, and how chromatin remodeling dysfunction contributes to disease in neuronal cells.

Assaf Vardi

Plant & Environmental Sciences

KEYWORDS

- Algal blooms
- Marine viruses
- Oxidative stress
- PCD
- Pathogenic bacteria
- Cell-cell communication

WHAT

Marine Microbiology

HOW

The role of cellular mechanism, signaling and metabolic crosstalk in mediating microbial interaction (host-virus, host-bacteria, predator-prey) in the marine environment

MODEL ORGANISM

Phaeodactylum tricornutum, thalassiosira pseudonana Emiliania huxleyi sufitobacter Emiliania huxleyi virus

MAJOR METHODS

- Single cell RNAseq
- Cell imaging microfluidics
- Flow cytometry
- Mass spectrometry- metabolomics
- Redox signaling

The Vardi Laboratory aims at exploring the cellular mechanisms involved in sensing and acclimation to diverse environmental stress conditions during algal bloom dynamics in the ocean. Our research utilizes the recent advances in the field of chemical ecology (metabolomics and Mass spectrometry imaging) combined with single cell imaging and transcriptomic approaches to track cell-cell interactions at the micro(be)-scale. We study key biotic interactions (host-virus, host-bacteria, predator-prey and allelopathy) that regulate the fate of algal blooms, in order to discover novel signalling and metabolic pathways employed during these interactions. Newly identified genes and metabolites induced during specific host-pathogen interactions are used as functional biomarkers to assess the ecological impact of microbial interactions in structuring microbial food webs and potentially global nutrient cycles.

Talila Volk

Molecular Genetics

KEYWORDS

- Mechanotransuction
- Muscle
- Nuclear membrane
- LINC complex
- Lamin

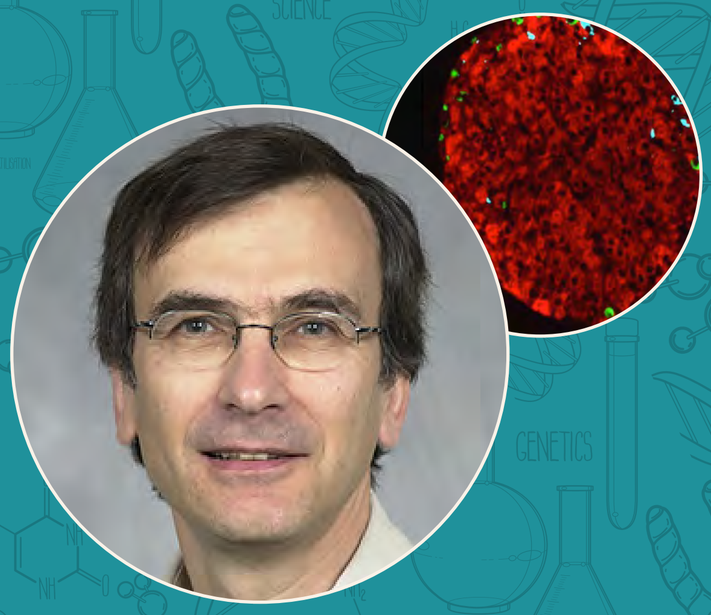
WHAT Cell and developmental biology

HOW We study how mechanical signals on the nuclear membrane affect the chromatin in muscle fibers

MODEL ORGANISM *Drosophila melanogaster*

MAJOR METHODS Advanced microscopy, Quantitative high resolution imaging, smFISH, genetic approaches, protein analysis

Contractile muscle fibers are multinucleated cells with highly organized cytoplasm and characteristic connections with tendons required for proper muscle function. Our lab studies mechanical aspects of muscle development using the fruit fly Drosophila as our major animal model. Major research topics studied in the lab: (1) The 3D architecture and epigenetics of muscle nuclei. (2) Nuclear mechanotransduction and its effect on cell cycle. (3) Dynamic measurements of nuclear deformations in response to force manipulations.



Michael Walker

Biomolecular Sciences

KEYWORDS

- Pancreas
- Islet
- Diabetes
- Transcription
- Metabolism

WHAT The pancreatic β cell in health and disease

HOW The goal of our research is to understand how pancreatic beta cells perform their unique functions

MODEL ORGANISM Mouse

MAJOR METHODS Cell culture, measuring gene expression, analyzing genetically modified mice

Pancreatic beta cells are the only cell type capable of producing the key metabolic hormone insulin: their function is essential for normal metabolic balance, and their dysfunction is central to the development of both major forms of diabetes.

In our research, we focus on the following aspects of beta cell function:

1. The transcriptional mechanisms underlying the normal embryonic development of beta cells and the functioning of mature beta cells
2. Manipulating pancreatic cellular identity: molecular mechanisms controlling exocrine to endocrine cell reprogramming
3. Dissecting the signaling mechanism that permit beta cells to respond to modulators of insulin secretion, in particular long chain and short chain fatty acids

Karina Yaniv

Biological Regulation

KEYWORDS

- Zebrafish
- Blood vessel
- Regeneration
- Organogenesis
- Vascular

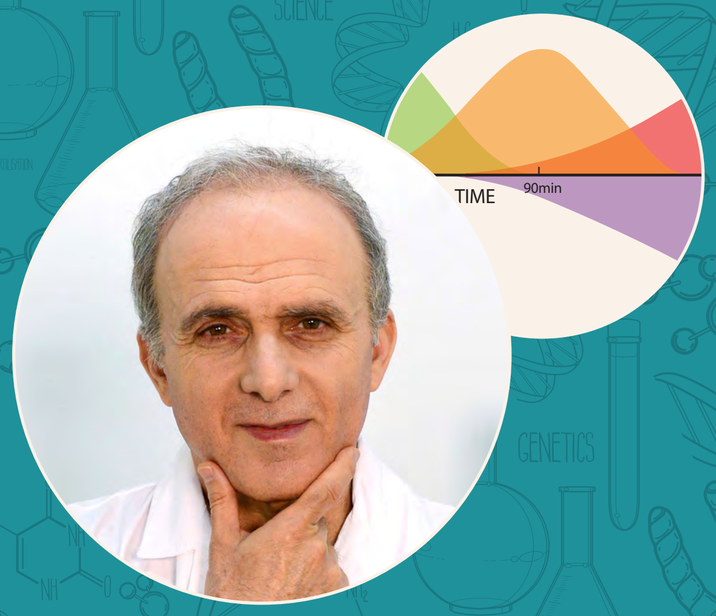
WHAT Vascular biology, organ development and regeneration

HOW Blood and lymphatic vessel formation during embryonic development, organ regeneration and disease

MODEL ORGANISM Zebrafish

MAJOR METHODS Live Imaging, Drug Screens, Crispr/CAS mutagenesis, genomics

Development of multicellular organisms is a complex process that requires several events of cellular proliferation, differentiation and organization to be executed in a stereotypic order. As development proceeds, progenitor cells undergo progressive fate decision steps, each refining their identity, until they reach a functional end state. Our work aims at understanding how endothelial cells become specified to generate functional blood and lymphatic vessels that support organogenesis and regeneration. To this end, we use the zebrafish, a transparent vertebrate, which on top of enabling high-resolution live-imaging and easy genetic manipulations, are able to regenerate most of their organs.



Yosef (Yossi) Yarden

Biological Regulation

KEYWORDS

- Drug development
- Growth factors
- Metastasis
- Signal transduction

WHAT Cancer progression, metastasis and therapy

HOW We use animal models and genomics to resolve cancer mechanisms and ways to block them using novel drugs

MODEL ORGANISM Mice (both immunocompromised and immunocompetent)

MAJOR METHODS Molecular biology, RNA sequencing, monoclonal antibodies, pharmacology

While the majority of tumors are initiated by genetic aberrations, all malignant lesions follow a subsequent step-wise progression phase, which involves growth factors. Unlike many oncogenic mutations, growth factors and their receptors are amenable to pharmacological interception. We focus on the group of EGF-like growth factors and their ERBB/HER family receptors. We study the principles of signal transduction networks and focus on the complex transcriptional programs that underlay EGF-to-ERBB signaling. This understanding offers opportunities for pharmacological targeting growth factor signaling, experimental strategies to retard metastasis and ways to overcome resistance to cancer therapies.

Yifat Merbl

Immunology

KEYWORDS

- Proteasome profiling
- Immunoproteomics
- Immunotherapy
- Cancer
- Autoimmunity

WHAT	Systems Immunology, Biochemistry, epiProteomics
HOW	Proteostasis control in cancer and immune regulation
MODEL ORGANISM	Mice, Humans
MAJOR METHODS	Proteasome Profiling, Mass spectrometry, biochemistry, immunology, in vivo models

Standing at the intersection of immunology, biochemistry, and proteomics, our lab studies **proteostasis regulation in cancer and immunity**. We focus on elucidating regulatory mechanisms involving protein modification and degradation in biochemical, cellular and physiological levels. We utilize immuno-proteomics, cell biology, in-vitro and in-vivo models to reveal novel control mechanisms of protein modification and degradation across different disease models. We combine our expertise to gain insight into basic and translational questions and develop cutting-edge technologies in epiProteomics and biochemical immunology to promote precision medicine and impact human health.

Avraham Yaron

Biomolecular Sciences

KEYWORDS

- Neurobiology
- Neurodevelopment
- Axon degeneration
- Axon guidance

WHAT	Mechanisms of neuronal wiring
HOW	Genetic manipulations of the mouse embryo and neuronal cultures
MODEL ORGANISM	Mouse
MAJOR METHODS	Mouse genetics, gene editing, neuronal cultures, microscopy

The wiring of the nervous system during development sets the pattern of connections that allow the organism to function in the world. This developmental program is composed of progressive events as guidance of axons to their targets, and regressive events in which axons and neurons are eliminated. Inappropriate execution of this program is in the basis of many neurodevelopmental disorders. In the lab we are studying the cellular and molecular mechanisms that control the wiring process through the use of in vitro neuronal cultures and the analysis of mutant mice.

Ada Yonath

Structural Biology

KEYWORDS

Ribosomes

Antibiotics

Resistance

Evolution

Nucleic Acids

WHAT

Ribosomes function; Defected ribosomes in human diseases; Novel eco-friendly antibiotics; Origin of life

HOW

Mutated ribosomes structural analysis, Design of novel antibiotics, Prebiotic peptide bond formation

MODEL ORGANISM

Bacteria, parasites, diseased human cells

MAJOR METHODS

- Isolation of ribosomes from pathogenic bacteria and from healthy or disease carrying human cell by sucrose gradient ultracentrifugation
- Structure determination of normal, mutated and modified ribosomes by high-resolution Cryo-EM techniques
- Revealing mutations in ribosomal components by mass spectrometry
- Design of compounds complementing specific structural motifs of pathogens mainly by antisense technology following biochemical assays for detecting their protein synthesis inhibition
- Construct functional RNA ”pockets”, similar to the highly conserved ribosomal active site, resembling the prebiotic peptide bond formation machinery

We are striving to reveal ribosomal structural elements that are linked to medical issues and to origin of life. Specifically:

1. Combating antibiotic resistance by designing next generation, eco-friendly novel antibiotics that target pathogen-specific structural motifs.
2. Studying mutated ribosomes that are associated with human diseases, anemia & cancer, aiming at removing or reducing tumor size alongside remote sensing of cancerous cells or metastases in body fluids.
3. Extending our studies, which suggest that the ribosomal site of peptide bond formation, a highly conserved pocket-like RNA feature, evolved from a prebiotic synthetic machinery, thus linking the RNA world and modern life.

Elazar Zelzer

Molecular Genetics

KEYWORDS

- Scoliosis
- Dysplasia of the hip
- Musculoskeletal assembly
- Morphogenetic mechanisms

WHAT Musculoskeletal development and disease

HOW Understanding the molecular and biomechanical principles governing musculoskeletal development and disease

MODEL ORGANISM Mice

MAJOR METHODS CRISPR/Cas9, single-cell analysis, proteomics and transcriptomics. advanced imaging modalities, high-throughput computer vision algorithms

The musculoskeleton is a tremendously sophisticated and complex biomechanical organ system. It allows vertebrates, including us humans, to display a vast repertoire of movement and postural patterns and, consequently, of behaviors and functions. Our main goal is to understand the biological and biomechanical principles governing musculoskeletal development and function, maintenance and regeneration, as well as aging and pathology. Deciphering the mechanisms underlying these processes will pave the way for development of new therapeutic approaches for treatment of numerous musculoskeletal diseases, including congenital and degenerative, and injuries.

David Zeevi

Plant & Environmental Sciences

KEYWORDS

Computational biology

Evolution

Pollution remediation

Microbiome

Ecosystem stability

Machine learning

WHAT Environmental microbiology, AI

HOW We study how microbes adapt to human-made pollution in order to find new ways to treat it

MODEL ORGANISM Environmental microbes

MAJOR METHODS

- Machine learning
- Multi-omic analysis
- High throughput screening
- Systems biology
- Environmental sampling

We study how microbial ecosystems are affected by human-made artifacts. We apply the insights learned from these microbes to devise new ways to protect the environment. We take two complementary approaches:

First, we use metagenomic and metabolomic assays, combined with AI, to find new genes that microbes use to evade and metabolize pollutants. Using high throughput screening and automation we validate our findings in the lab.

Second, we study the stability of microbial ecosystems and how it is affected by human-made perturbations, in order to predict and prevent ecosystem collapses. We use simple experiments, sampling of natural microbial populations, and machine learning models.

Yaniv Ziv

Neurobiology

KEYWORDS

- Calcium imaging
- Hippocampus
- Learning
- Memory

WHAT	Neural coding of long-term memory
HOW	We study the mechanisms and neural coding dynamics underlying long-term memory
MODEL ORGANISM	Mouse
MAJOR METHODS	Optical imaging, optogenetics

We are interested in how memory information is coded in the brain, and about what happens, from the neural code's perspective, to information "stored" in the brain over timescales that range from days to months. We investigate how memory information is coded by large neuronal populations in brain circuits that are important for memory processing. We do that by combining novel in-vivo optical imaging methodologies for longitudinal recordings of neuronal activity in freely behaving rodents, with genetic tools for manipulating specific molecular pathways or spiking activity in specific cell types, and behavioral assays of learning and long-term memory.