
Ichilov
Scientific
Ecosystem

Oncology Division Research Labs

- Wolf-Rubinek lab
- Breast cancer translational research lab
- Neuro-oncology translational research lab
- Hub for physicians with relevant research questions

Who we are and our area of interest

Name of lab/Location	PI/Manager	Main Subjects in the lab
• Wolf-Rubinek lab • 10th floor, 1082	• Ido Wolf & Tami Rubinek (MD/PhD) • Keren Merenbakh Lamin	• Cancer, aging and metabolism • Mechanisms of drug resistance • What regulates metastasis tropism? • Interesting clinical questions

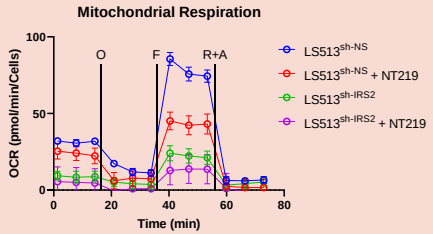
Key Capabilities

What are we specialized in

- **Using patients' clinical data and samples**
- **Cancer assays**: proliferation, migration, spheroid, etc.
- **Different tissue environments in vitro**: brain, liver, lung
- **Mice models**: orthotopic, genetic, immunotherapy
- **Transcriptomic**: including FFPE
- **Metabolism**: seahorse, enzymatic assay, softwares
- Regulation of gene expression (shRNA)

What specialized equipment we use to answer Q

- ELISA reader
- <u>Equipment at TAU:</u>
- Seahorse
- Mass spec for metabolomics
- Illumina sequencing

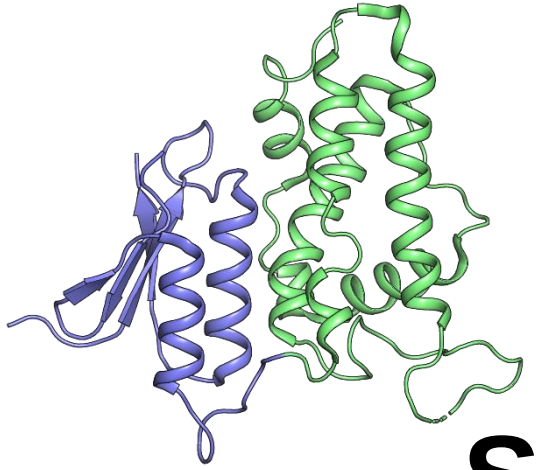
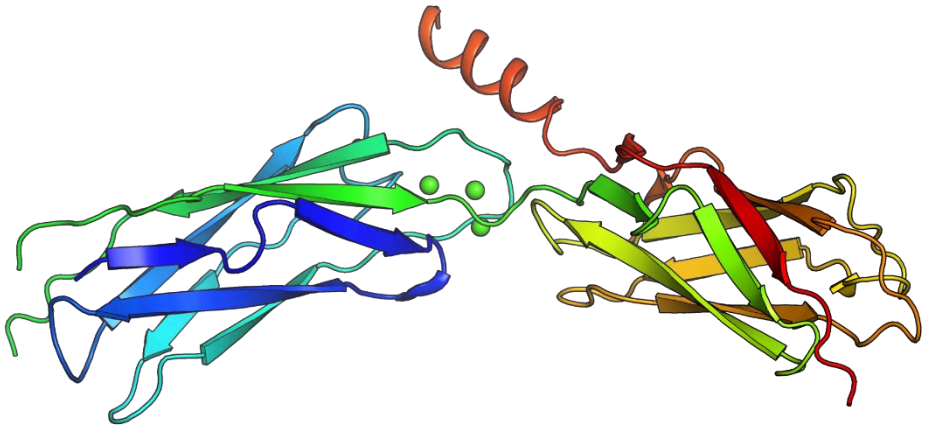
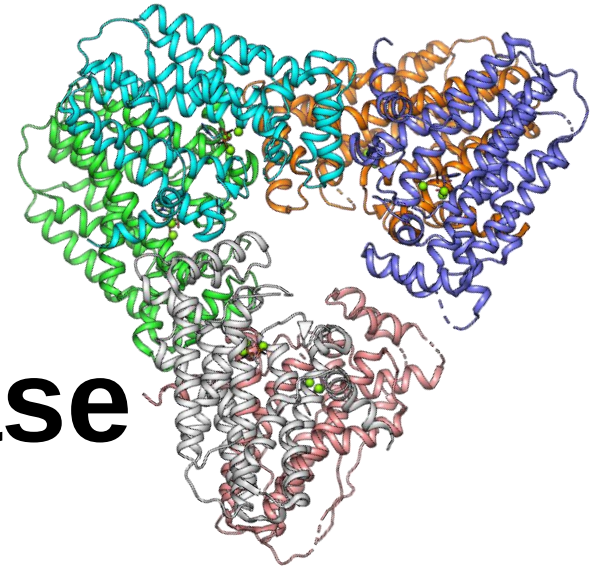


How can we aid other scientists to answer their Q

- Analyze metabolomics
- Seahorse
- Cancer-related assays
- Share clinical/molecular databases

What questions still needs to be answered, what is needed in order to answer them?

- Generation of in vitro systems simulating different tissues/metastatic sites i.e., liver, brain: bioprinter
- Spatial genomics, transcriptomics, proteomics
- Seahorse or other device to analyze metabolism
- **Bioinformatics:**
  - **for mining public databases**
  - **analyzing omic experiments**
  - **Structural biology**

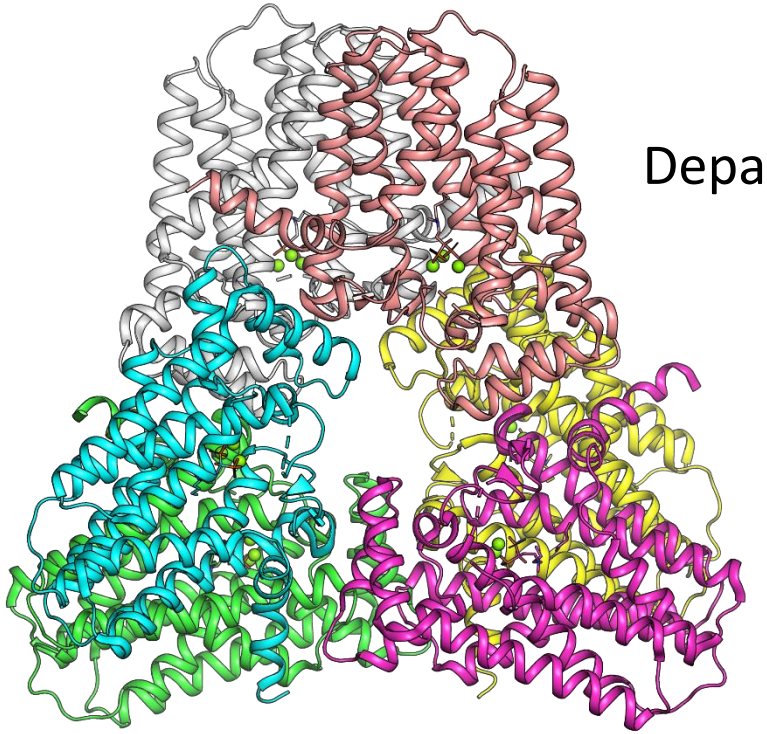
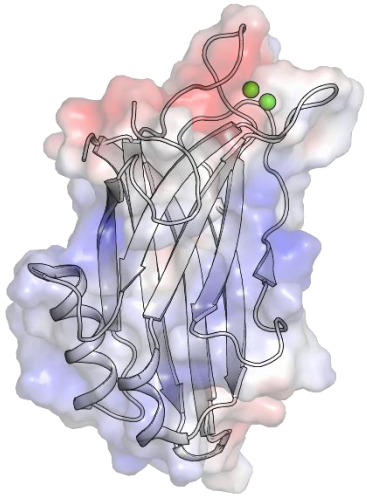
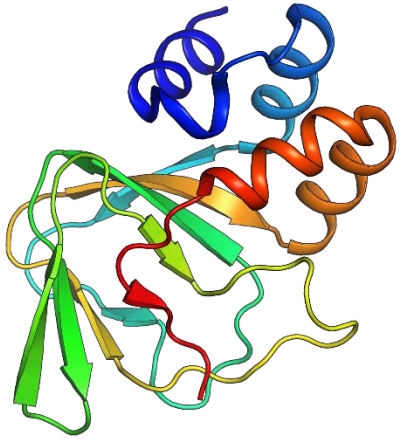
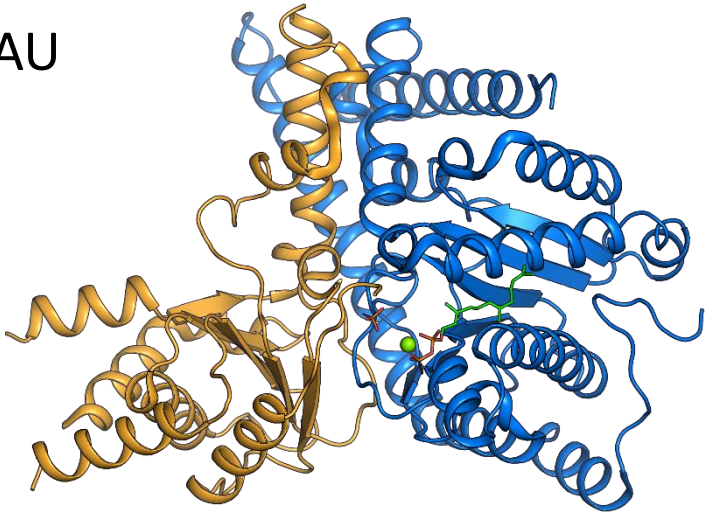




Structural biology of disease

Moshe Giladi

Internal Medicine D, TASMC

Department of Physiology and Pharmacology, TAU

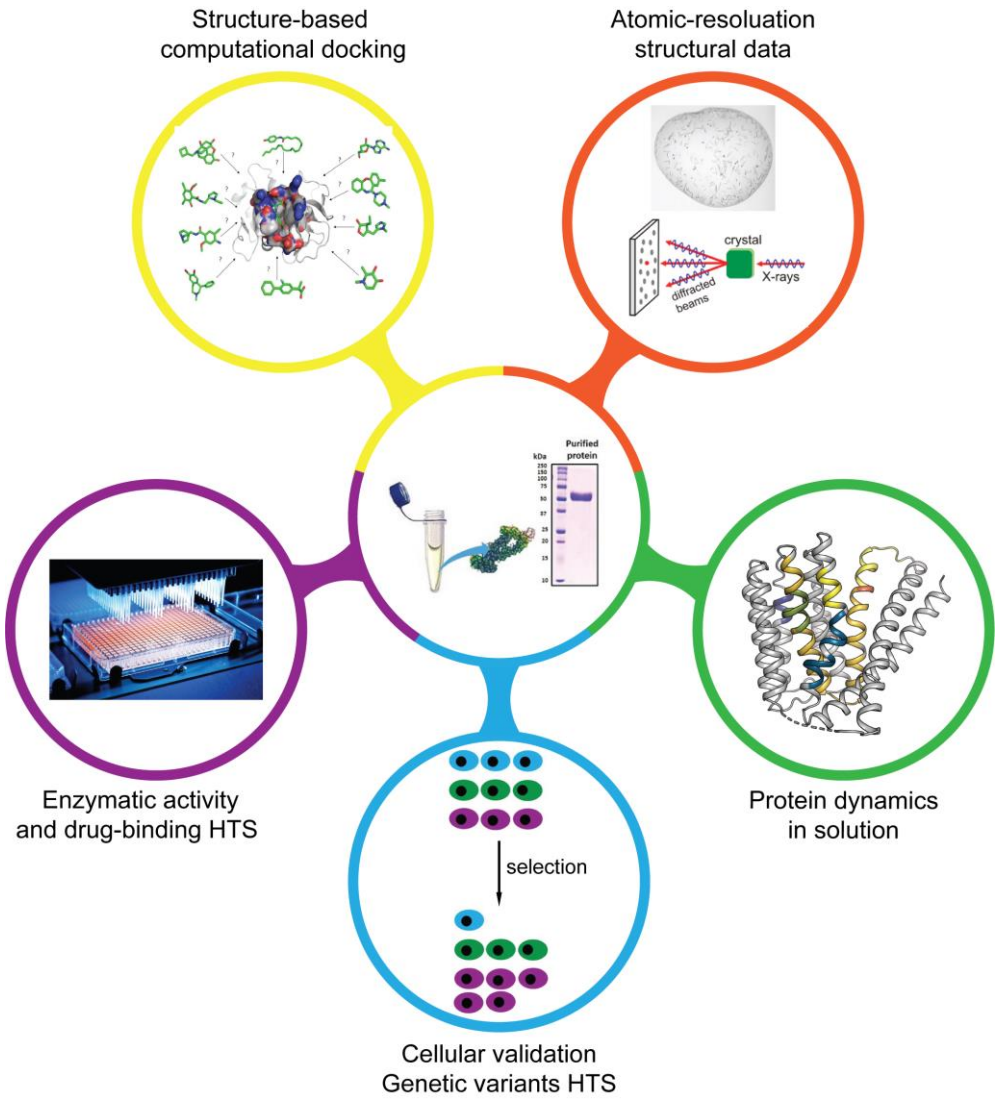
Who we are and our area of interest

Name of lab/Location	PI/Manager	Main Subjects in the lab	Keep it simple to people who are not in the field
• Structural biology of disease	• Moshe Giladi	• Structure-function studies of proteins involved in human diseases • Molecular docking • High-throughput drug screening	• **Function follows structure.** We study proteins structure to understand their function in health and disease and develop new therapeutics.

Key Capabilities

What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Protein purification • X-ray crystallography • Structural modeling • Molecular dynamics • Computational docking • Fluorescence spectroscopy	• High-performance GPU • Large-scale bacterial cultures and processing (future) • AKTA FPLC system (future)	• Protein structure modelling • Predicting effects of novel variants • Mechanistic insights from molecular simulations • Small-molecule docking

Experimental approach



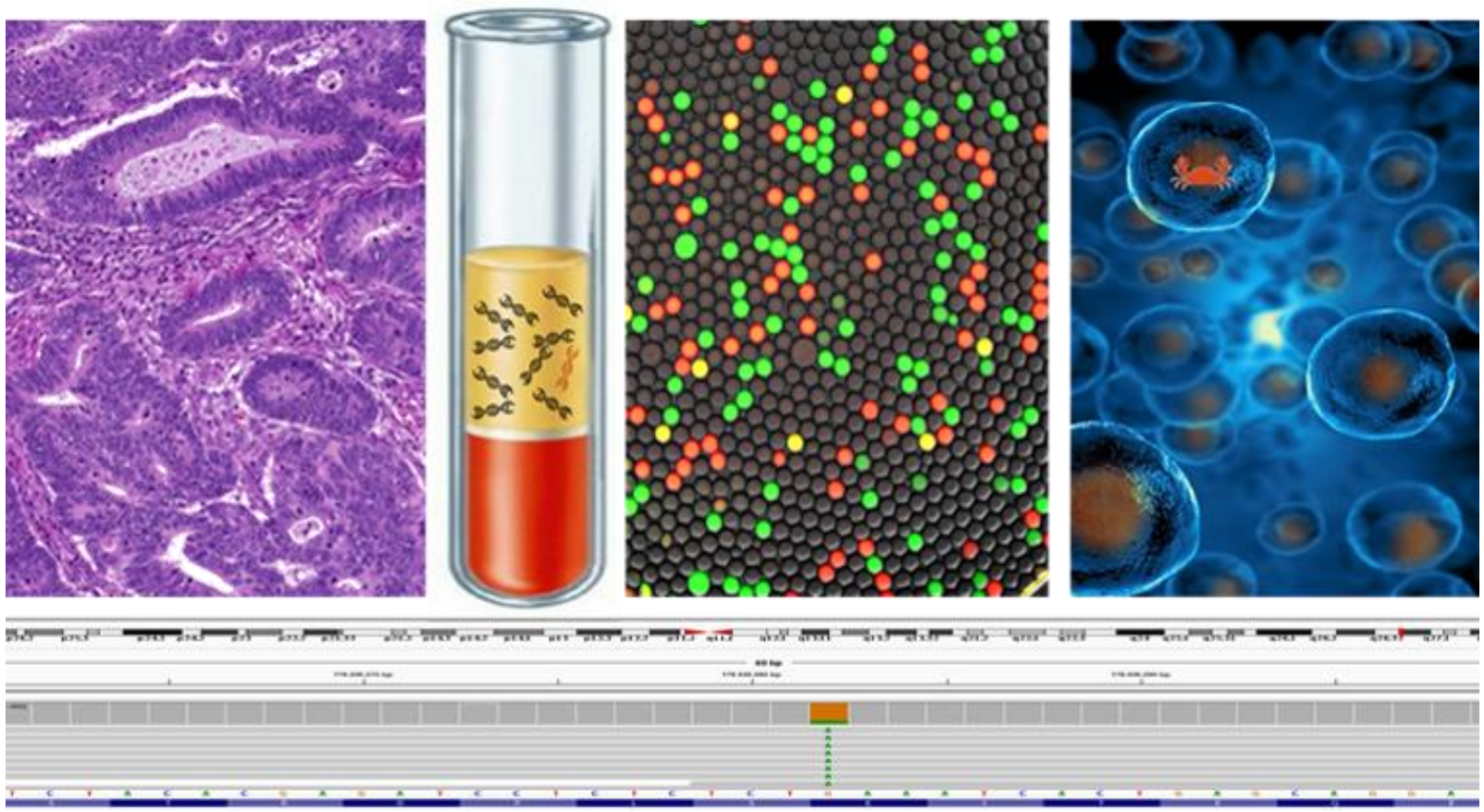
What questions still needs to be answered, what is needed in order to answer them?

- What is the structural basis for allosteric interactions in oligomeric enzymes?
  - High-throughput yeast-based phenotypic analysis platforms
- How *de novo* mutations affect protein structure and result in human diseases?
  - Protein purification pipeline
- How can post-translational modifications be targeted in different cancers by small molecules?
  - Multimode microplate reader for small molecule HTS

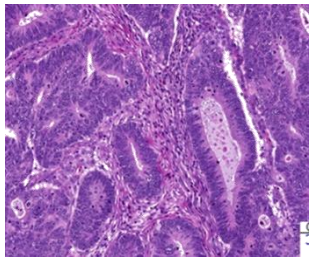
Pathology research lab

PIs':
Prof. Dov Hershkovitz
Dr. Shlomo Tsuriel

Victoria Hannes
Bat-El Gabay
Noa Papo
Chen Weizmann



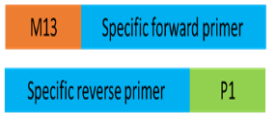
Liquid biopsy – patient specific consume NGS panel



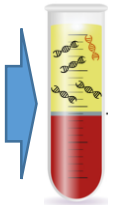
Patients diagnosis with LARC

Tumor genetic >500 genes screen

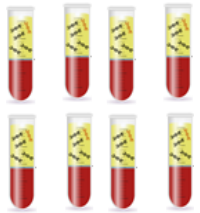
Mutations detected



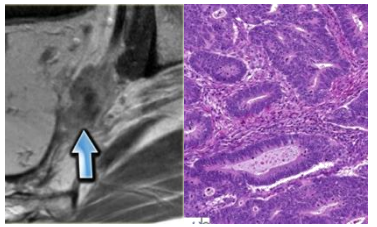
Mutation specific panel design



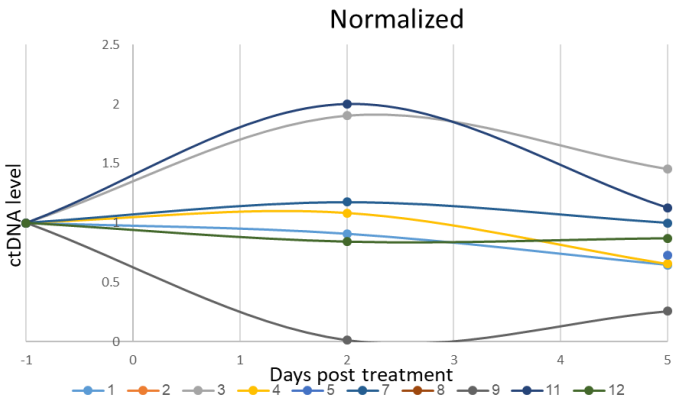
Pre treatment plasma



Plasma every visit on the first weeks and then once a week



Post surgery tumor assessment



Pathology-AI research center

Multiple scanning platforms
Strong IT

Clinical team

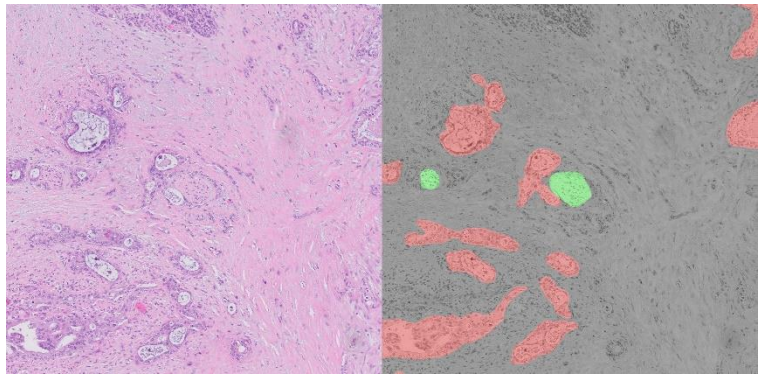
Industry

Imagene

CODE FOR ISRAEL

רשות החדשנות
Israel Innovation
Authority

Algorithmic team



Who we are and our area of interest

Name of lab/Location	PI/Manager	Main Subjects in the lab	Keep it simple to people who are not in the field
• Pathology research lab • Cancer biomarkers	• Prof. Dov Hershkovitz • Dr. Shlomo Tsuriel	• Liquid biopsy • Developing new molecular tools • Digital pathology	• Liquid biopsy- we know to build patient specific NGS panel and to detect low frequency mutation and MRD • We design and validate new molecular tools based on NGS or digital PCR to gain better tumor diagnosis • Digital pathology – using AI tools to improve diagnosis, assist the pathologist and identify new biomarkers

Key Capabilities

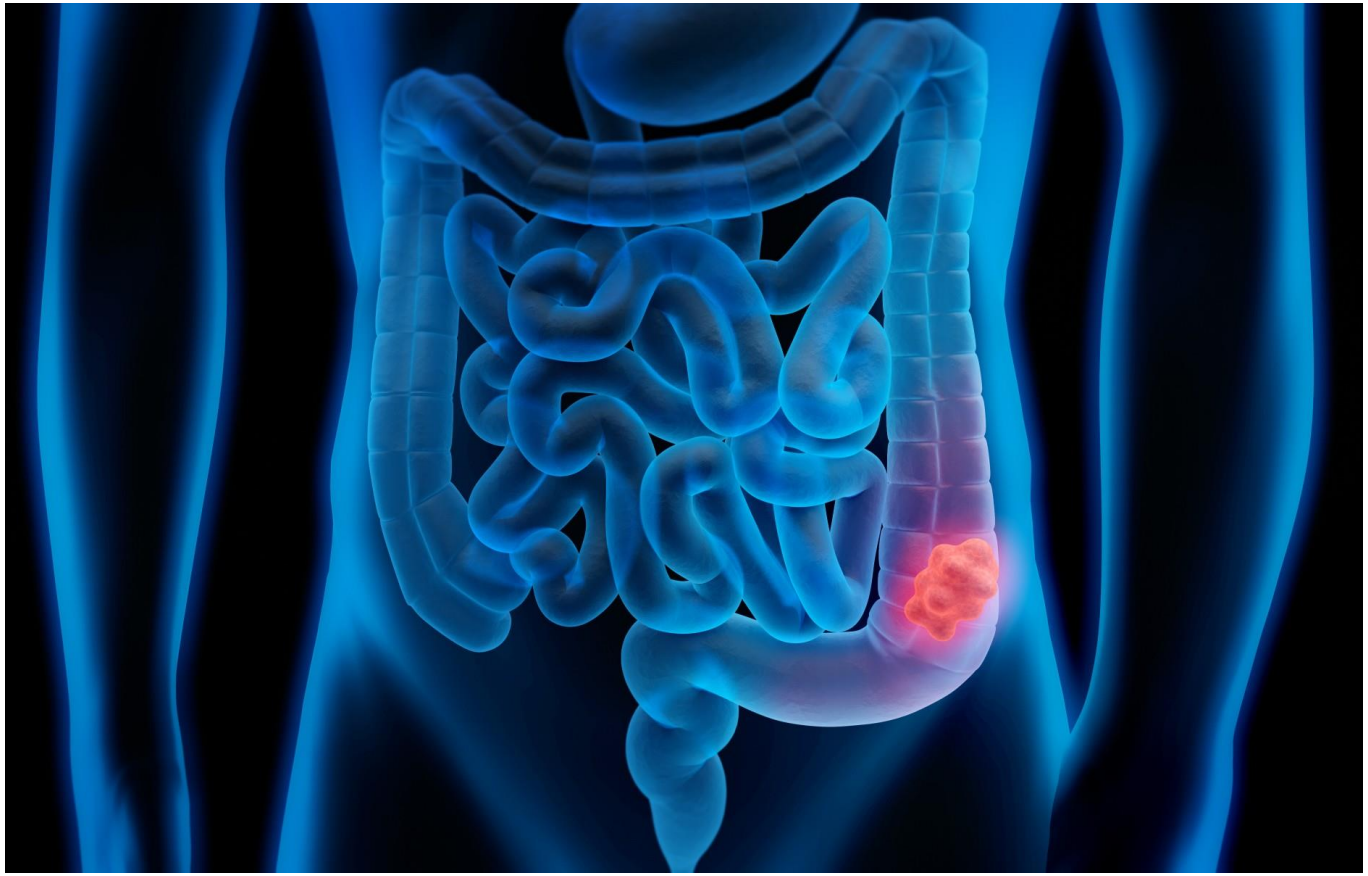
What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Somatic NGS • Liquid biopsy • Designing small NGS panels • Image analysis • Deep learning, based image segmentation	• Pathology archive • Ion torrent sequencing machines • Digital PCR • DNA/RNA extraction from FFPE. • IHC facility (Ventana and DAKO platforms) • Digital pathology scanners allowing high resolution scanning of histology slides	• Helping with designing small NGS panels including interpretation of the results. • Building digital PCR assays and using our digital PCR • Access to the pathology database. • Scanning and interpretation of histology slides.

What questions still needs to be answered, what is needed in order to answer them?

- Question: Can we predict treatment response using high resolution liquid biopsy?
  - High resolution samples from patients undergoing treatment.
  - Bioinformatics expert
- Question: How to improve automatic segmentation and quantification of histomorphological elements?
  - Image analysis experts

The Surgical Oncology Lab

Dr. Eran Nizri
Kelly Lipczyc



Who we are and our area of interest

Name of lab/Location	PI/Manager	Main Subjects in the lab
• Surgical Oncology Lab • Sammy Ofer 10th floor, room 64-65	• Dr. Eran Nizri (PI) • Kelly Lipczyc (Manager)	• Biomarkers for efficacy of heated intra-peritoneal chemotherapy (HIPEC) • Biomarkers for severe post-operative complications • Immunological response to peritoneal metastasis from colorectal cancer • Personalized 3D-printed scaffold for tissue regeneration

Key Capabilities

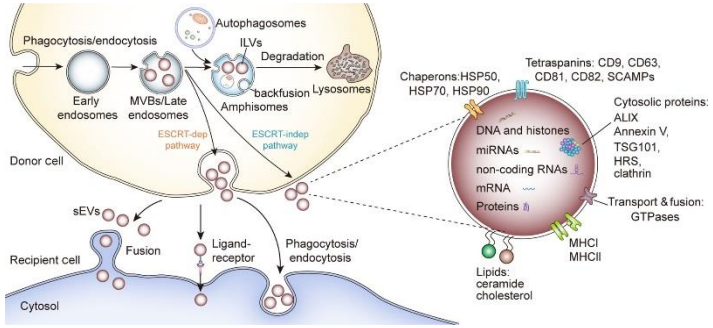
What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Working with human samples • Research of the tumor immune micro-environment • Cytokines quantitation • Working with polymers	• IHC • Flow cytometry / sorting • RTPCR • Elisa • We developed a mouse model of peritoneal metastases	• Immunology • FACS

What questions still needs to be answered, what is needed in order to answer them?

- We need experience with 3D cell culture and tissue regeneration

Who we are and our area of interest

Tumor-Microenvironment cellular interactions in cancer progression and metastasis



Name of lab/Location	PI/Manager	Main Subjects in the lab
• Surgical Oncology Research Lab • Sami Ofer building 10th floor rooms	• PI: Guy Lahat • Manager: Shelly Loewenstein	• Cross talk between GI cancer cells and cells of the peritoneal microenvironment (adipocytes, mesothelial and endothelial cells) mediated by extracellular vesicles (EVs) • EVs as biomarkers and therapeutic nanoparticles • Obesity and cancer • Soft tissue sarcoma and EVs

Key Capabilities

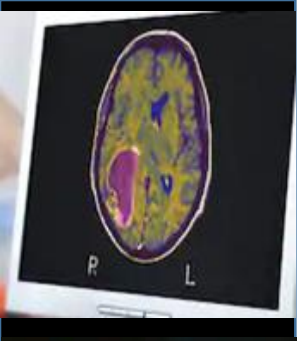
What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Extracellular Vesicles(EVs) • Tumorigenesis in vitro assays (proliferation, trans well migration and invasion, apoptosis assay, cell cycle) • Angiogenesis tube and plug assays • MiRNA isolation from cells, plasma, FFPE and EVs • MiRNA manipulations • Adipose tissue explants • Primary adipocytes isolation and differentiation (3T3-L1) • Tumor xenografts models	• Ultracentrifuge • Nanosight • qRT-PCR • FACS • ELISA • IHC • Confocal microscopy • IVIS	• Teach EVs practice • Different in vitro tumorigenic assays • MiRNA • shRNA knock downs • Adipose tissue culture (omentum)

What questions still needs to be answered, what is needed in order to answer them?

- CRISPER KO
- Metabolic assays
- Culturing patients primary tumor cells
- Orthotopic mice model-gastric cancer
- Bioinformatics experts

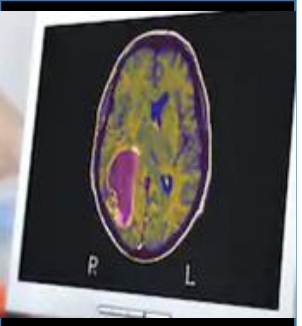
Neuro-Oncology Translational Research Lab

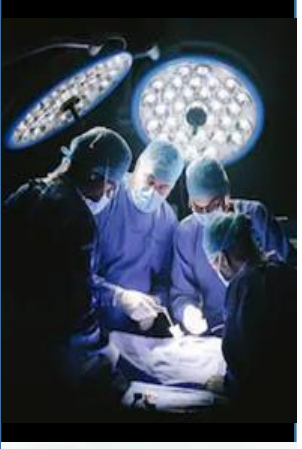
Name of lab/Location	PI/Manager	Main Subjects in the lab	Keep it simple to people who are not in the field
Lab: Sami Ofer 10th floor, room 91 (affiliated with Oncology lab) & **Clinic**: Radiotherapy Institute (Sourasky wing A floor -2)	Co-PIs: **Dr. Leor Zach** Head of Neuro-Radiotherapy Unit **Dr. Orit Furman** Head of Lab	• Research in a multi-disciplinary environment, including medical and radiation oncologists, pathologists, radiologists, neurosurgeons, neurologists, physicists. • **1st Project: Predict response to RT in Lung cancer Brain Mets based on pre-treatment MRI and radiation plans.**	• **Our questions come from the clinic.** • We want to make use of big-picture viewpoint to identify methods for better diagnosis, personalized treatment, QOL of people with brain tumors



Key Capabilities

What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Looking at brains • Analyses of Radiotherapy–related data • Novel MRI-based analysis methods (Treatment Response Analysis Maps) • Generating computerized patient DB from multiple hospital computer systems.	• Unique access to RT data, generated from advanced radiotherapy equipment, including MRI-guided radiotherapy. • We are involved in establishing the National Proton Therapy Institute in TASMC	• Thinking outside the box • Help you build your patient DB using RedCap in TASMC. • Multi-disciplinary collaborations





What questions still needs to be answered, what is needed in order to answer them?

- We want to be create a digital platform that will enable clinicians and researchers to look at the combination of clinical data, brain MRI, digital pathology, multi-omics data & neuro-cognitive assessments in order to identify which treatment protocols are working for which cohorts of patients.
- We want to combine whole-genome DNA methylation sequencing of brain tumors with RT treatment and MRI data in order to learn about differences in the biology of specific sub-types of brain tumors between patient cohorts (e.g. older and younger patients). This has implications on treatment options.

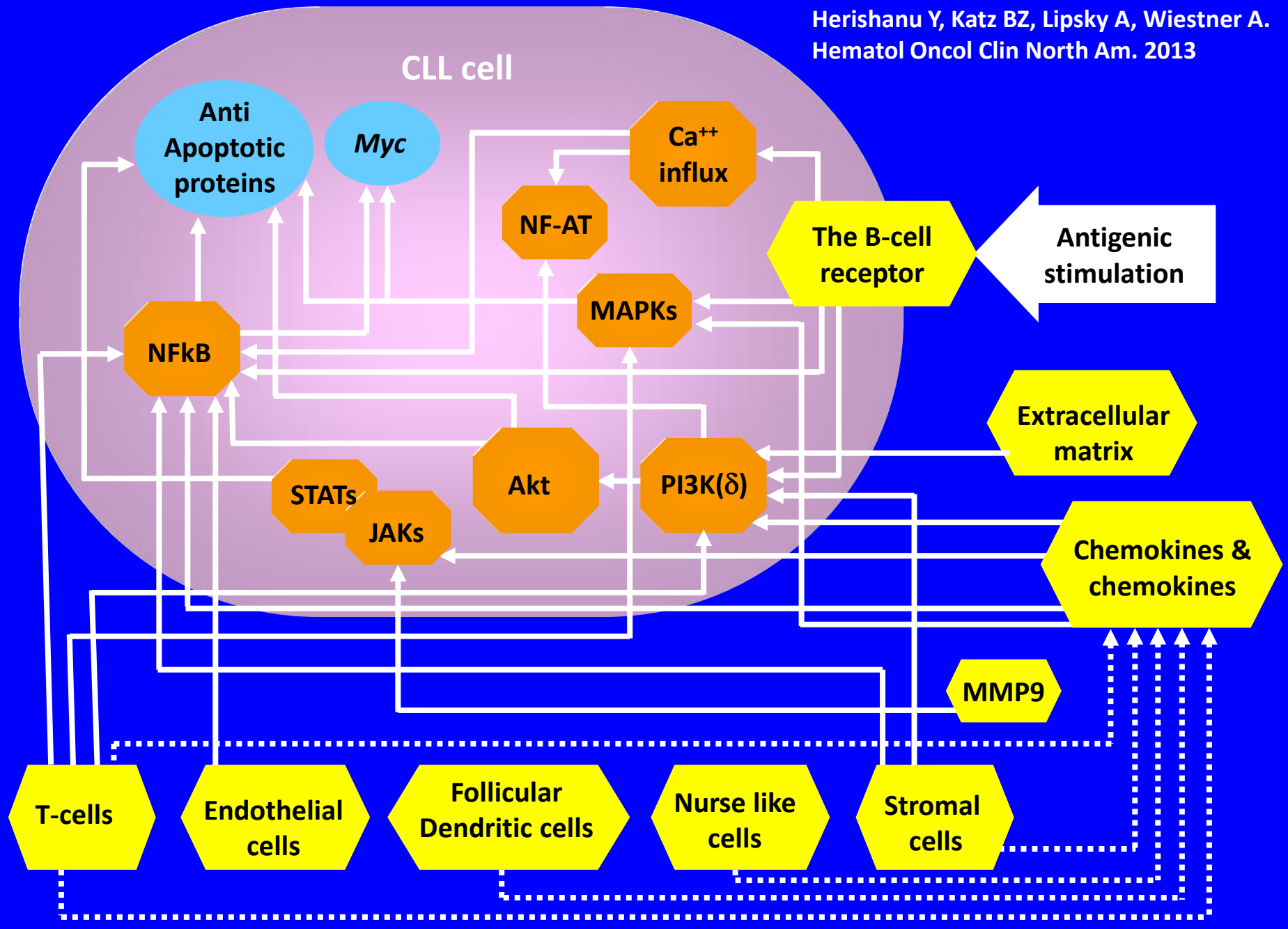
- **We need better access to IT infrastructure** to work in-house on patient-related TASMC data.
- **We need access to computational scientists** in fields such as bioinformatics, artificial intelligence, MRI advanced methods analysis, physicists.

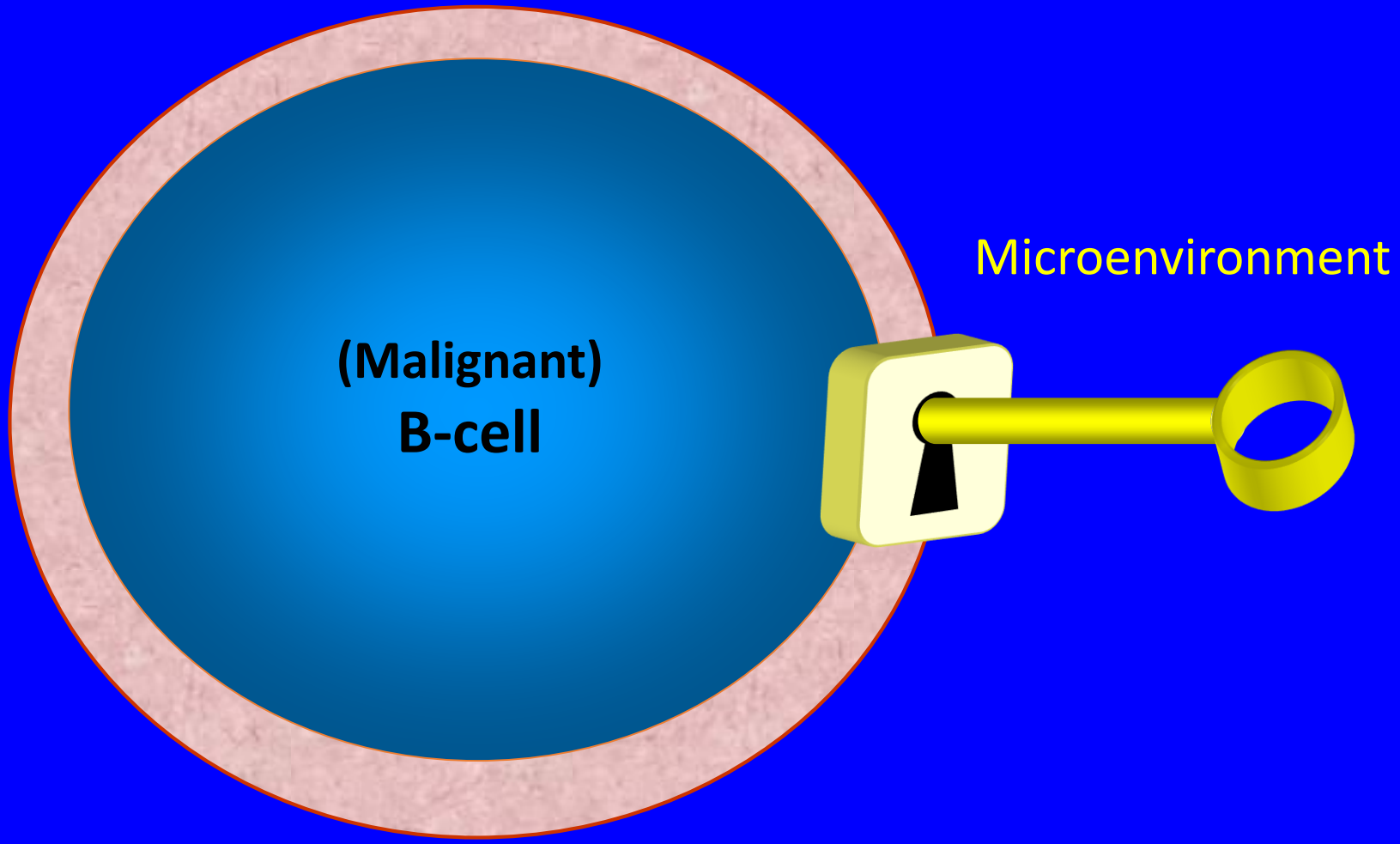
Chronic Lymphocytic Leukemia

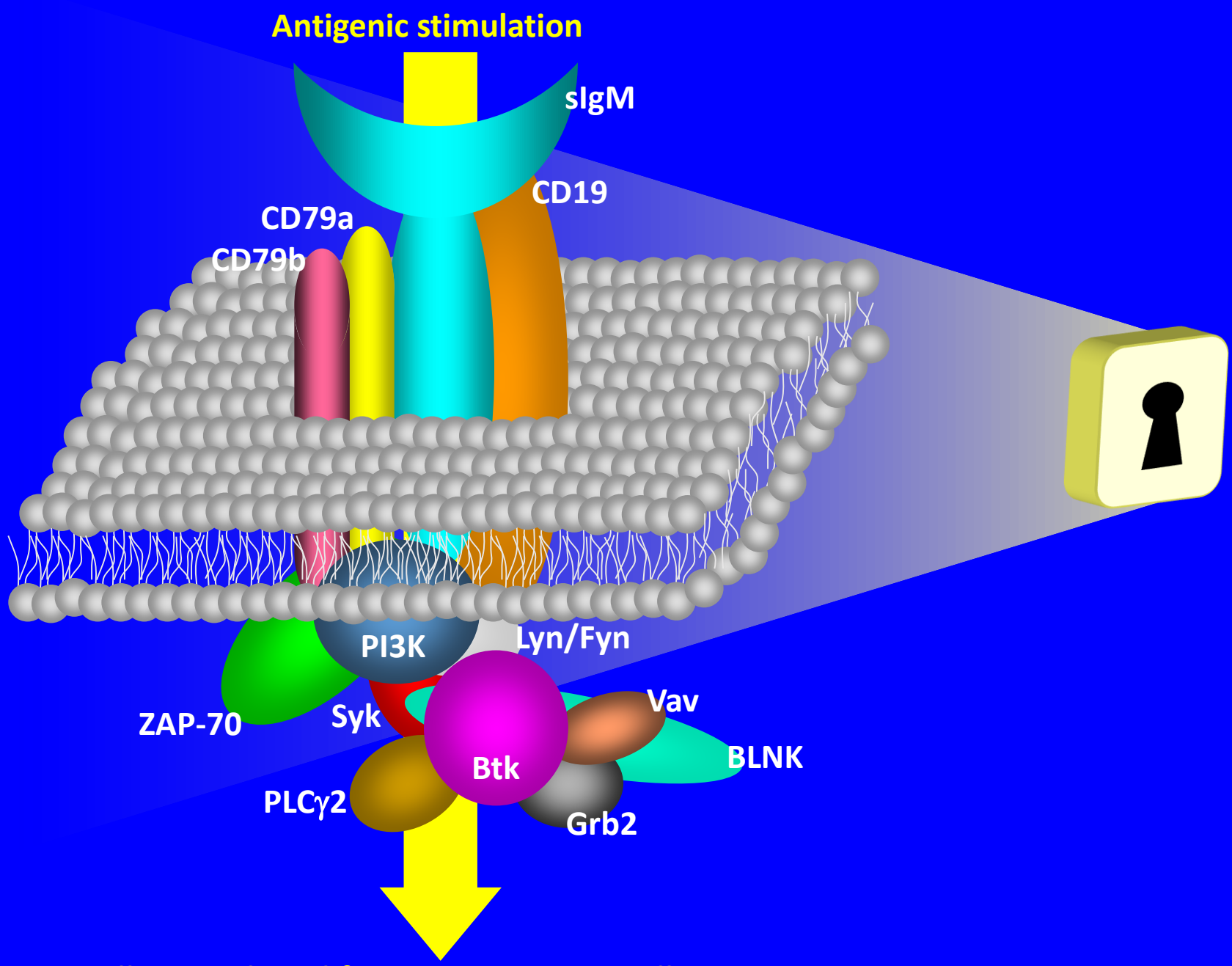
- CLL is an indolent lymphoproliferative disorder
- The most common leukemia in Western countries
- Progressive accumulation of monoclonal $CD5^{+}CD19^{+}$ B-cells, in the peripheral blood, bone marrow and lymphoid organs
- Heterogeneous clinical course

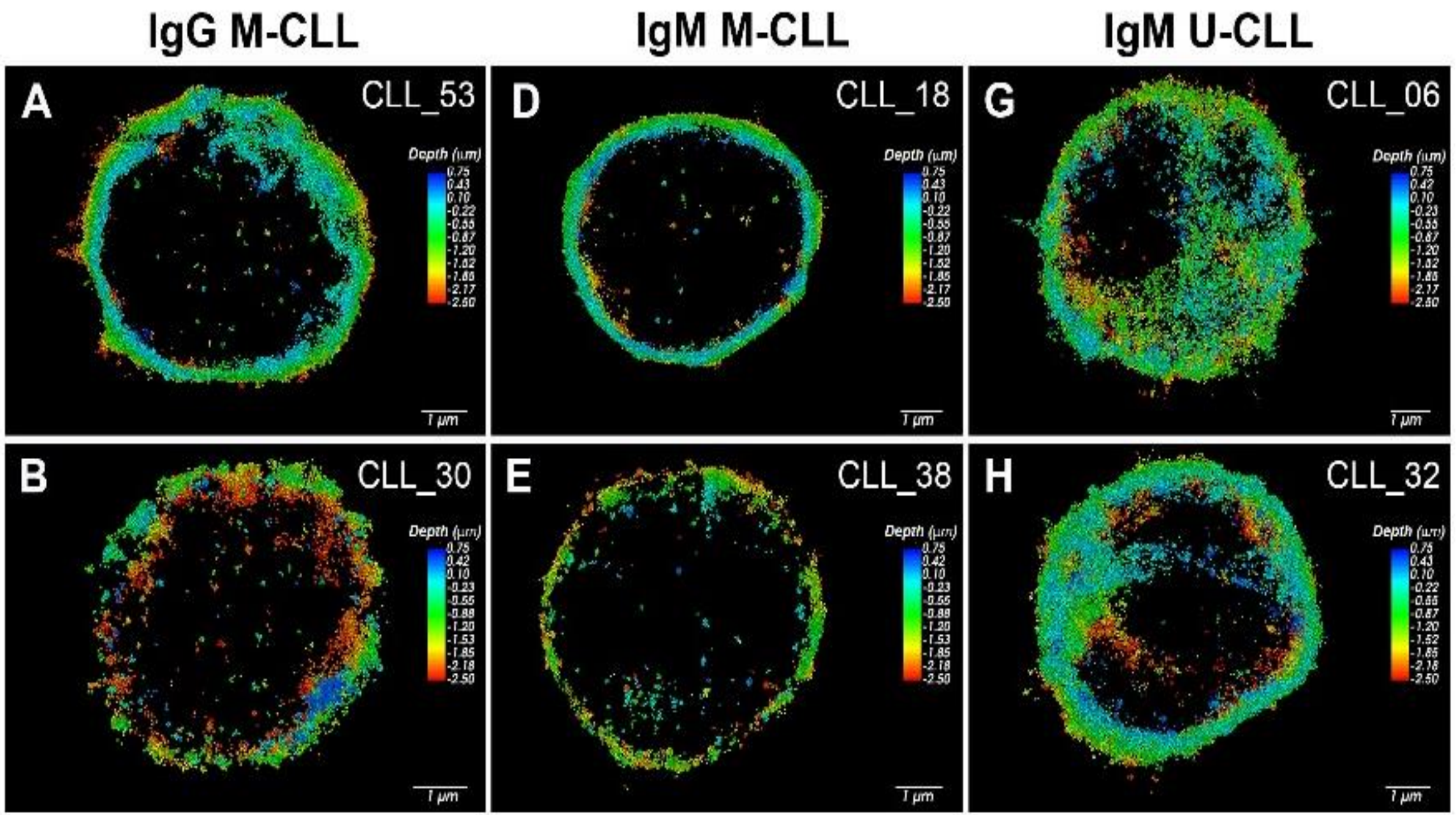
The microenvironmental signalosome in CLL

Herishanu Y, Katz BZ, Lipsky A, Wiestner A.
Hematol Oncol Clin North Am. 2013




(Malignant)
B-cell
Microenvironment

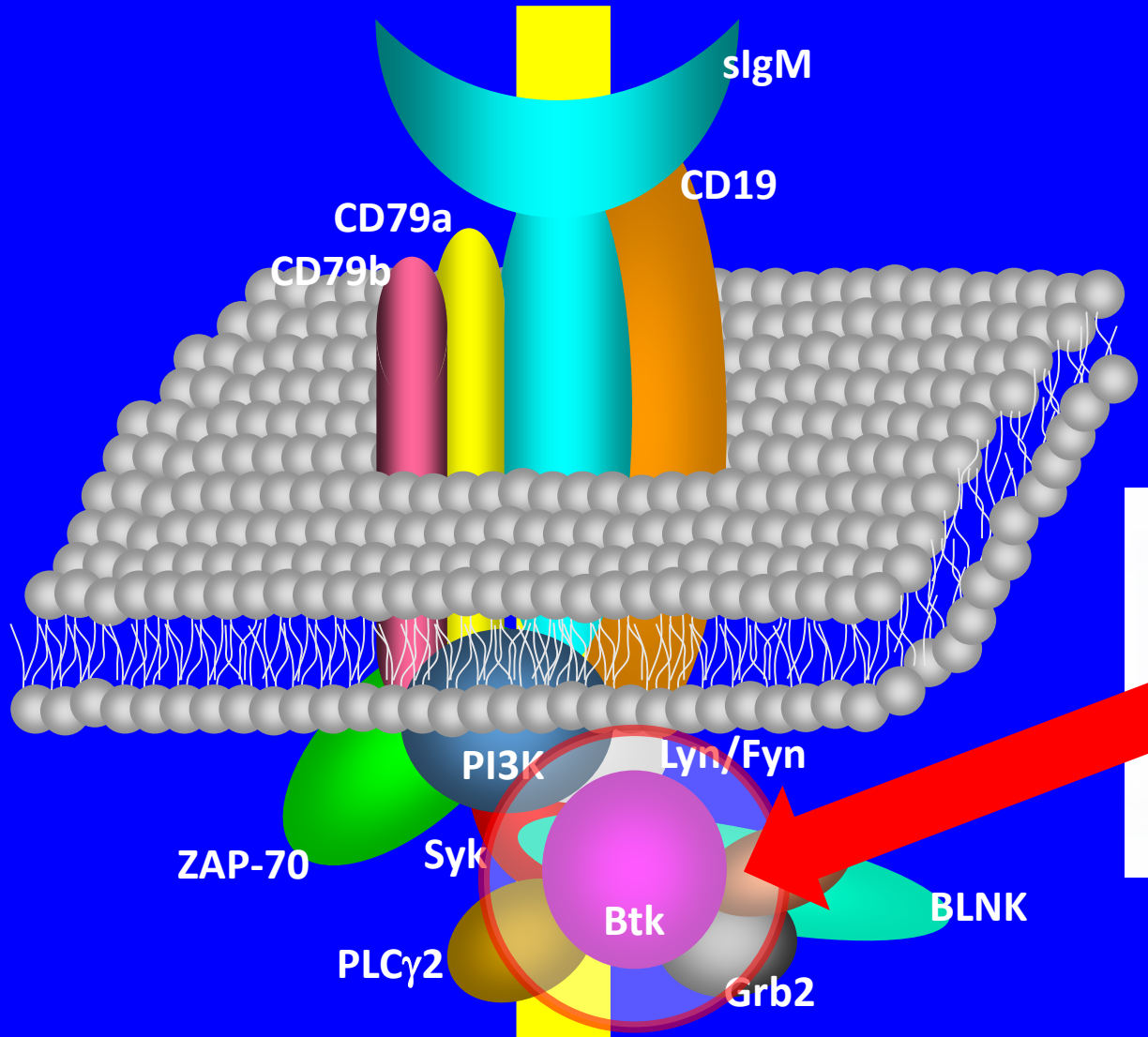

Antigenic stimulation
sIgM
CD19
CD79a
CD79b
PI3K
Lyn/Fyn
ZAP-70
Syk
Vav
BLNK
Btk
PLCγ2
Grb2
CLL cell survival, proliferation, migration, adhesion


IgG M-CLL
IgM M-CLL
IgM U-CLL
A
CLL_53
D
CLL_18
G
CLL_06
B
CLL_30
E
CLL_38
H
CLL_32
Depth (µm)
1 µm

Who we are and our area of interest

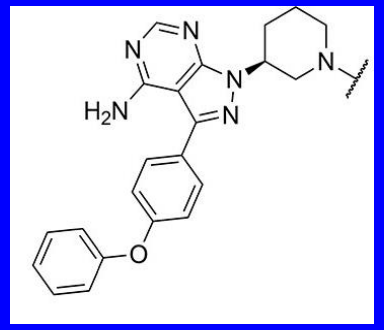
Name of lab/Location	PI/Manager	Main Subjects in the lab	Keep it simple to people who are not in the field
• Hematology Cancer Research Laboratory (10th floor)	• Yair Herishanu • Benzi Katz	• Elucidation of BCR signaling mechanisms in chronic lymphocytic leukemia • Targeting of BCR signaling in CLL by novel therapeutics • Improvement of current therapeutics in CLL • Analysis of the microenvironment of CLL and its contribution to the pathophysiology of the disease • Quantitative morphological analyses of the blood elements	• Dissection of the B-cell receptor signaling cascades in chronic lymphocytic leukemia cells in order to understand the clinical behavior of the disease in specific patients, and to find novel therapeutic targets

שפעול הקולטן הראשי של תאי CLL

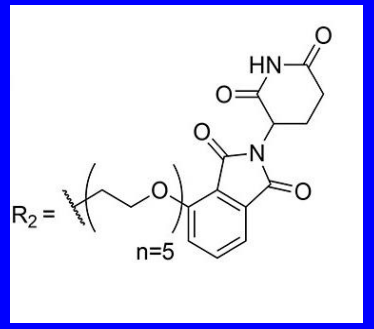


~~CLL שגשוג ונדידה של תאי~~

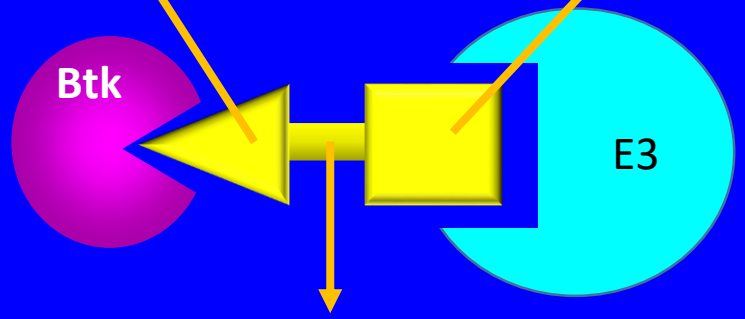
Ibrutinib

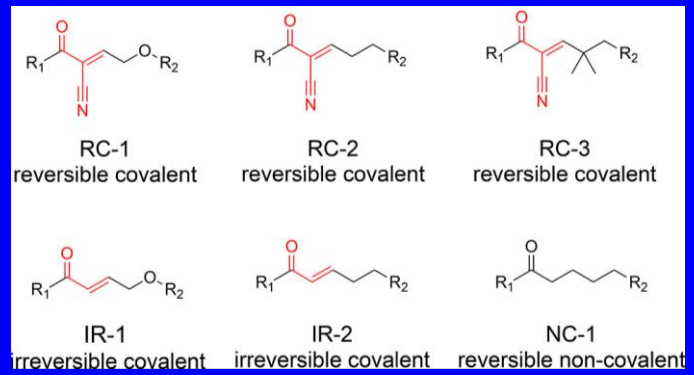


Thalidomide



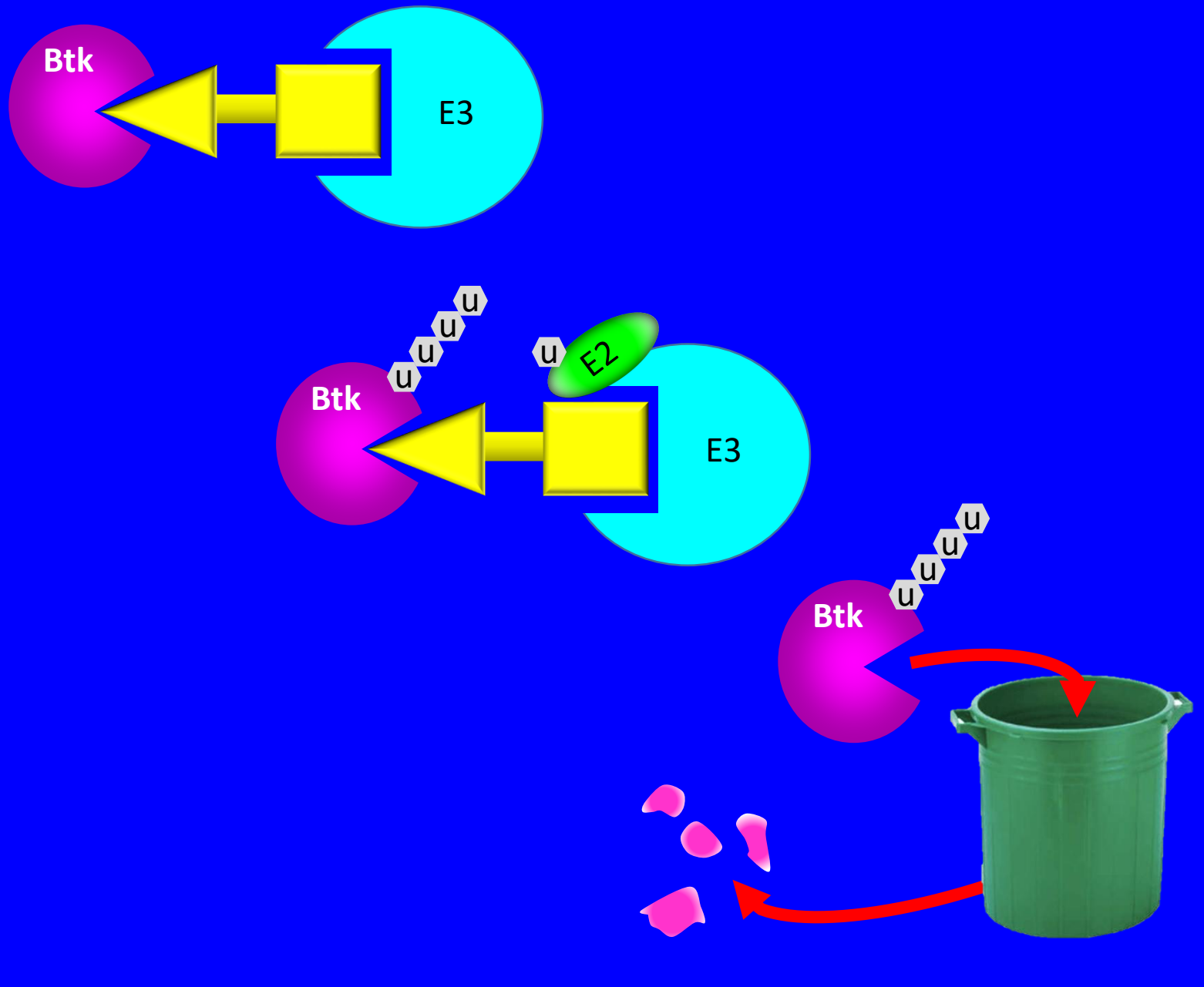
PROTAC





Linkers

הנדסת מולקולות


Btk
E3
u
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Btk
E2
E3
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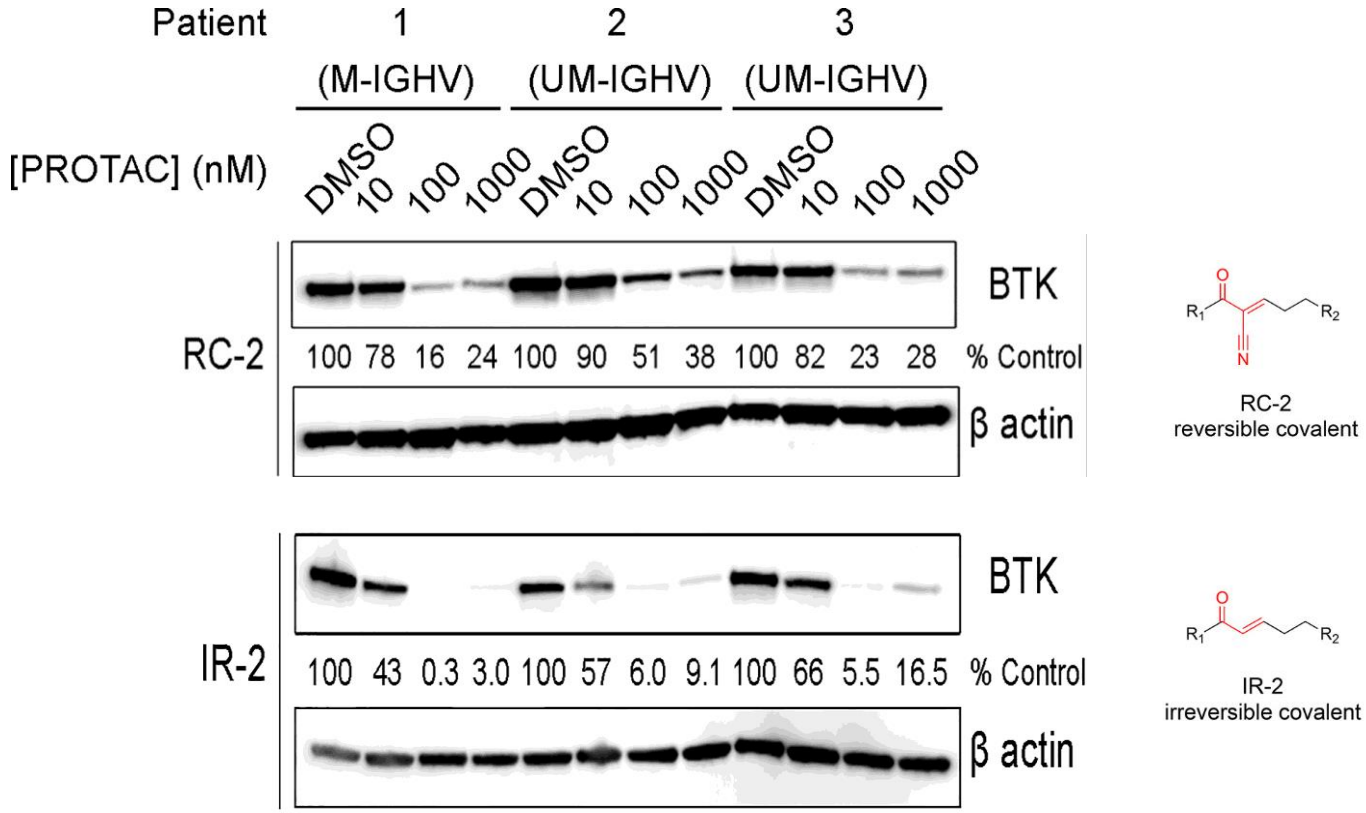
Btk

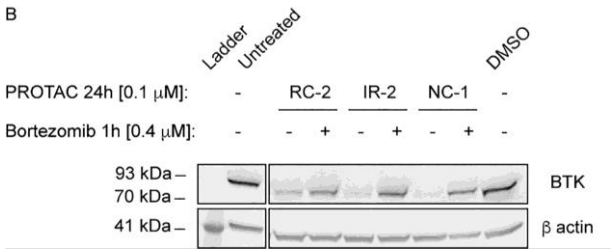
PROTACs degrades BTK in a protesome dependent manner



RC-2
reversible covalent

IR-2
irreversible covalent

Proteasome inhibitor



Gabizon R, Shraga A, Gehrtz P, Livnah E, Shorer Y, Gurwicz N, Avram L, Unger T, Aharoni H, Albeck S, Brandis A, Shulman Z, Katz BZ, Herishanu Y, London N. Efficient Targeted Degradation via Reversible and Irreversible Covalent PROTACs. J Am Chem Soc. 2020 Jul 8;142(27):11734-11742.

Key Capabilities

What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Protein analysis, including Western blotting, immunoprecipitation and flow cytometry • Preservation and propagations of primary CLL cells (bank) and various cells lines • Immunofluorescence approaches • Biological assays (e.g. cell migration, apoptosis, survival and activation) • Digital morphological analysis of routine PBS and BMA samples	• Western blotting techniques • Flow cytometry (core facility) • Immunofluorescence (TAU, WIS) • Single cells RNAseq (WIS) • Digital morphological analysis (the routine hematology laboratory)	• The effects of leukemic cells on the immune system (ongoing collaboration with Anat Globerson-Levin). • Analysis of signaling cascades. • Assessment of anti-leukemic activity of potential drugs (ongoing collaboration with Nir London, WIS). • Digital morphological analysis of clinical morphological PBS and BMA samples.

What questions still needs to be answered, what is needed in order to answer them?

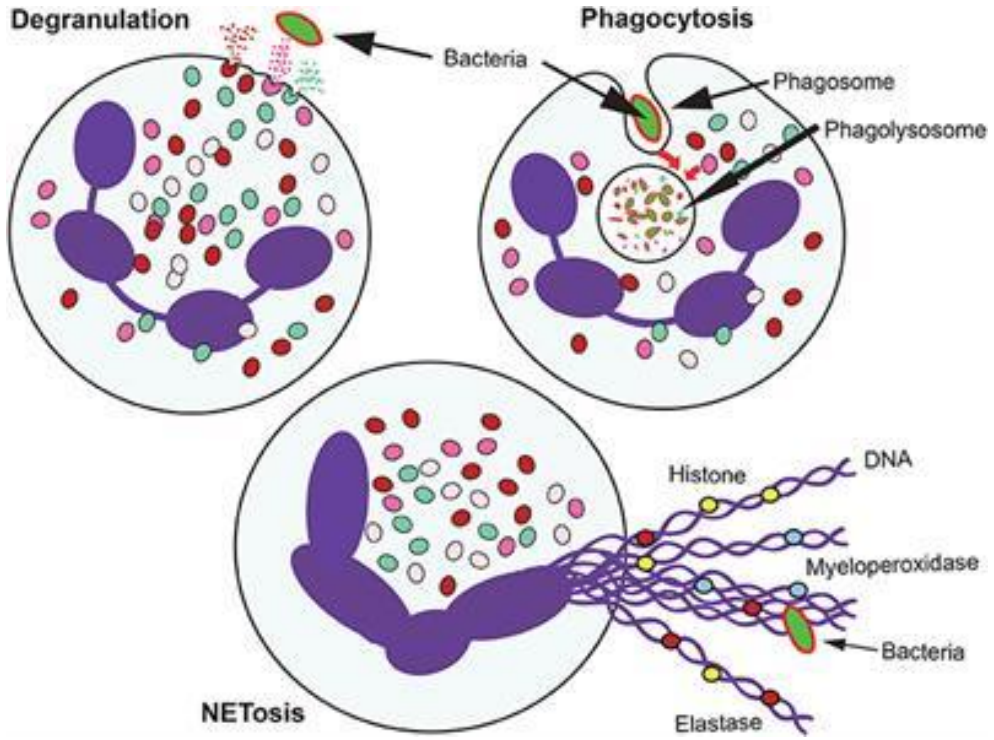
- What are the roles of specific molecules within the BCR complex in the regulation of CLL pathophysiology ?
- Protein analysis tools
- How CLL modulates the microenvironment ?
- Single cell RNAseq
- How CLL modulates the immune system, and how such effects can be overcome ?
- Flow cytometry, bioassays

Who we are and our area of interest

Name of lab/Location	PI/Manager	Main Subjects in the lab	Keep it simple to people who are not in the field
• Pediatric Hemato-Oncology Research Laboratory (Sammy Ofer, floor 10, room 61-62)	• Prof. Ronit Elhasid MD • Rachel Zicherman MD PhD • Szilvia Baron PhD (lab manager)	• Neutrophil function in pediatric cancers • Neutrophil function in inflammatory conditions in the pediatric population	• Novel prognostic markers and therapeutic targets in pediatric malignant tumors and inflammatory diseases

Neutrophils and their function

- Neutrophils - **innate immune system** – first line of defense
- Neutrophils protect against microorganism - by phagocytosis, release of cytotoxic molecules by degranulation, and release of **neutrophil extracellular traps (NETs).**
- Neutrophils – influence the **adaptive immune response** by interacting with T and B cells and antigen presenting cells (APC)
- NETs release - also in non-infectious conditions, like inflammatory disease, autoimmune diseases, thrombosis associated conditions and **cancer.**
- NETs release - promote **chemotherapy resistance** and **metastasis,** hence inhibition can be used for cancer therapy



Functional assays in our laboratory

- Enzymatic activity of **neutrophils elastase** (NE), **myeloperoxidase** (MPO) via colorimetric assay
- **Superoxide** and **ROS** production by FACS
- **Phagocytosis** by FACS
- **Degranulation**, detecting NE, MPO and MMP9 with ELISA
- **Neutrophil extracellular trap** (NETs) release using immunofluorescent staining (of isolated neutrophils and tissue samples) and imaging with confocal microscopy
- **Neutrophil extracellular trap** (NETs) from serum/plasma samples by ELISA

Current projects in our laboratory

Pediatric Cancers:

- Ewing's sarcoma – in collaboration with Tami Geiger, Clinical Cancer Proteomics, Weizmann Institute
- Medulloblastoma
- Osteosarcoma
- Lymphoma

Inflammatory disease:

- Inflammatory bowel disease (IBD) – collaboration with Pediatric Gastroenterology
- Juvenile idiopathic arthritis (JIA) – collaboration with Pediatric Rheumatology
- Obesity and failure to thrive in children – collaboration with Pediatric Gastroenterology

Others:

- Sleep deprivation and NETs formation

Key Capabilities

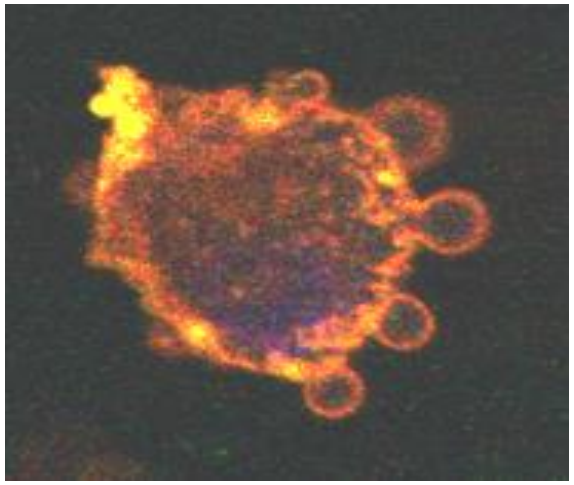
What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Neutrophil isolation • Neutrophil functions, NETs release • ELISA assays on serum samples • Immunofluorescent staining of human and mouse tissue • Confocal microscopy	• Easy Sep cell isolation system  • ELISA reader • Confocal Microscope • Incucyte S3 Live Cell Imager	• We are open for collaboration studying neutrophil function, specifically NETs release • We can advise on immunofluorescent staining and confocal microscopy

What questions still needs to be answered, what is needed in order to answer them?

- **Ewing's Sarcoma mouse model** – to check the effect of NETs inhibitors on chemotherapy resistance and metastasis
- **Neutrophil's role in the tumor microenvironment** – phenotyping tumor tissue samples, check possible interaction with T and B cells
- **Synergizing neutrophils and T cells in targeting poor-risk EWS** - for example CAR T secreting DNase

Extracellular vesicles
Tiny particles enormous impact

Ecosystem



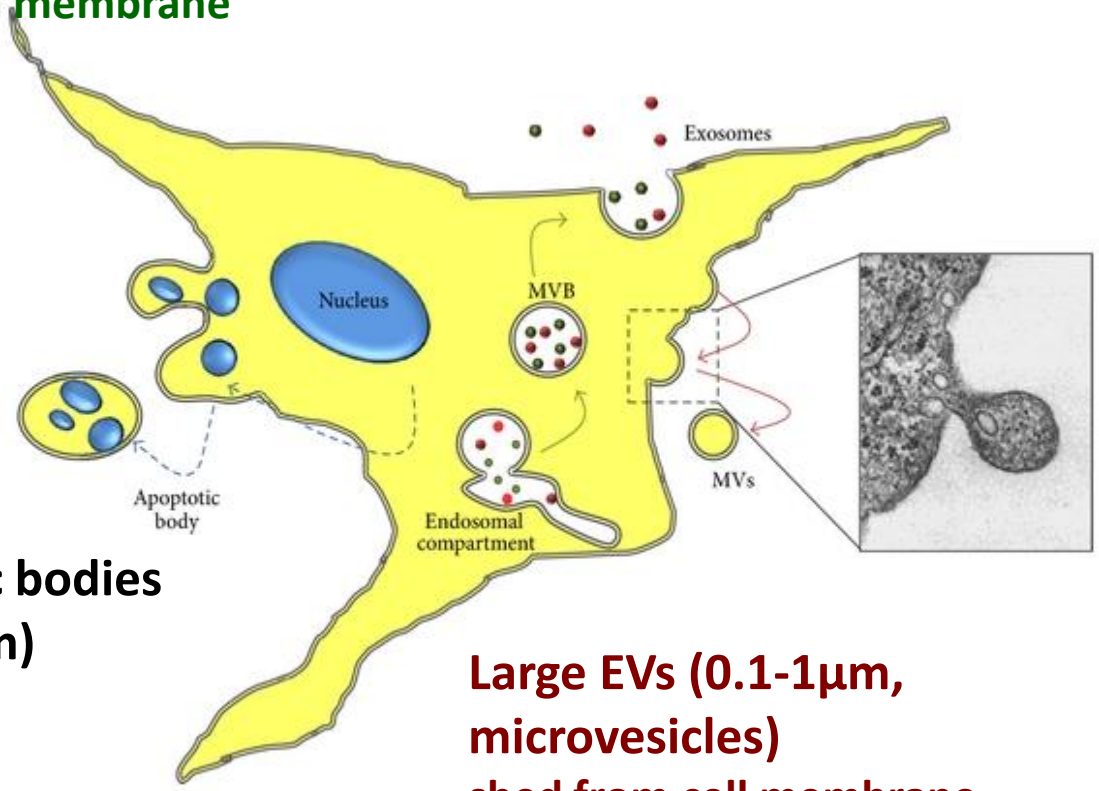
EVs shedding from Endothelial cell

Aharon A, Tamari T, Brenner B.
Thromb Haemost. 2008

Dr. Anat Aharon, PhD
Director of the Hematology Research Laboratory
Tel Aviv Sourasky Medical Center

Extracellular vesicles (EVs)

Small EVs (30-100nm, Exosomes):
Formed in the endosomal compartment, packed in multi-vesicular bodies and fuse with the plasma membrane

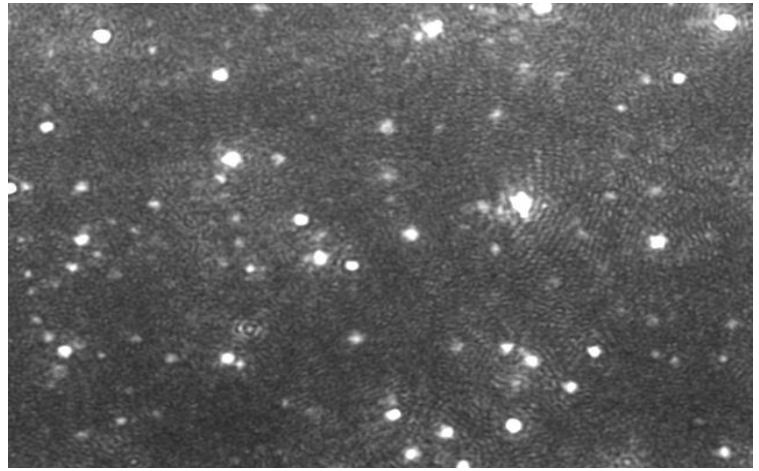


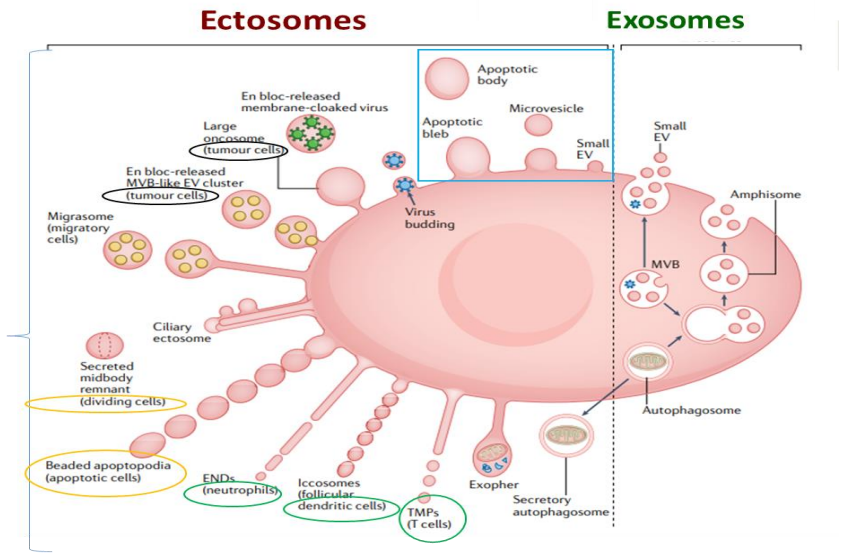
Apoptotic bodies (1µm-5µm)

Large EVs (0.1-1µm, microvesicles) shed from cell membrane

(Giusti, D'Ascenzo et al. 2013).

Nanoparticle Tracking Analysis (20-2000 nm)
~10^{11}EVs/ml plasma





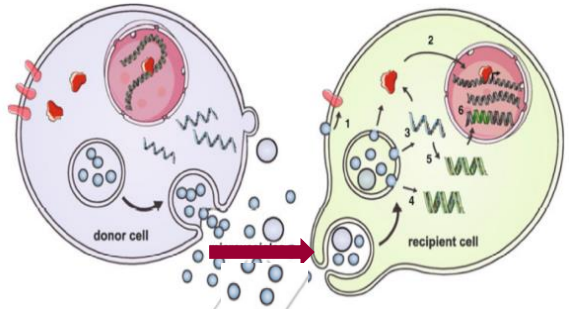
(Edit I. Buzas. Nature Reviews Immunology 2023)

Extracellular vesicles function

- EVs are found in body fluids of healthy individuals
  (plasma, urine, milk, etc.)
- Their levels increase in a variety of diseases
  (cancer, diabetes, vascular diseases, etc.)
  or following stimulation (chemotherapy, hypoxia..)

EVs play significant role in intercellular communication

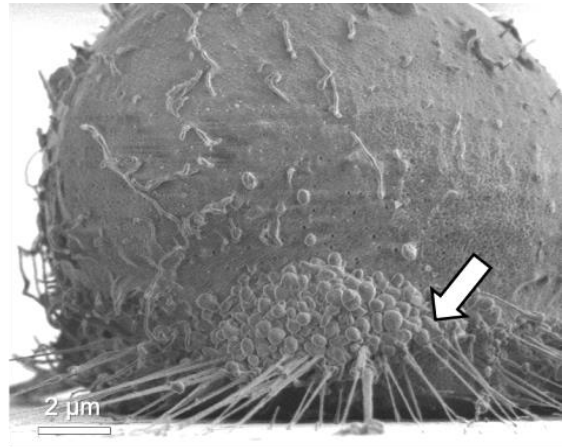
- EVs are involved in physiological processes
  (cell migration, invasion, angiogenesis)
- EVs can promote pathological states
  (thrombosis, inflammation, endothelial dysfunction)



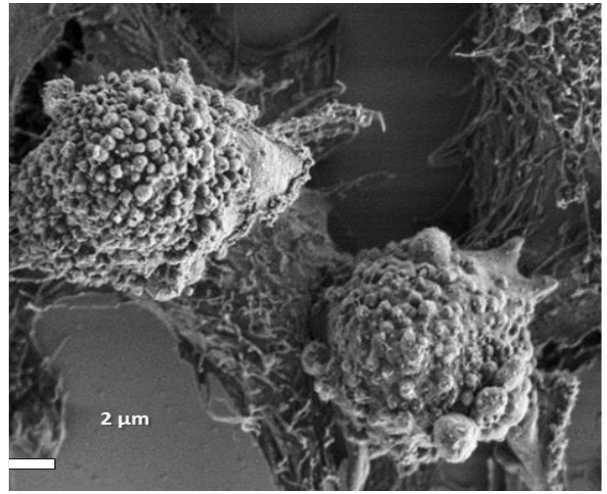
EVs may serve as valuable biomarkers for disease state and can use as therapeutic tool

Electron microscope scanning

Aharon A. Thromb.& Hem. 2018



Non-stimulated breast cancer cell line MDA231



Starved breast cancer cell line MDA231

Who we are and our area of interest

Lab mission :

- Defined EVs as biomarker for disease state & severity and efficacy of the treatment
- EVs as therapeutic tool - advantage compared to cellular therapy

Name of lab/Location	PI/Manager	Main Subjects in the lab	Research projects
Hematology Research Laboratory for Extracellular vesicles (EVs) Heart Building Floor 10, room 95	Dr. Anat Aharon	**EVs characterization:** • Size/Concentration • Structure • Membrane antigen, proteins content/function • DNA/miRNA content **EVs effect on cell cultures / mice models:** • EVs-cell interaction, • Apoptosis/Survival, • Migration, invasion, • Angiogenesis • Signal transduction	• CAR T EVs • Pregnancy & cancer • **Healing effects of Placental MSC EVs** in: i) cGVHD ii) Severe neonatal diseases iii)Lung fibrosis • COVIDE-19 patients (mild, moderate, sever and pregnant women vs. controls) • **Hematological malignancies** (Myeloma, AML, CNS lymphoma) • **Solid tumors** (breast, colon) • Gestational vascular complications • Neurodegenerative Diseases

Key Capabilities

What are we specialized in

- **EVs production**
- **EVs characterization**
- **EVs for cells / mice treatment**

What specialized equipment we use to answer Q

- Nano tracking analysis (NTA)

- Incucyte (live cell imaging analysis)

- Cytoflex (FACS)- Highly needed!!
- UC

How can we aid other scientists to answer their Q

EVs as biomarker:

i) For disease state & severity

ii) Efficacy of treatment

Resent projects:

- cGVHD (with Prof. Ron Ram)
- COVID-19 (with Prof. Giris Jacob)
- COVID-19 & Pregnancy (with Dr. Ayelet Dangot)

EVs as therapeutic tool:

- **CAR T EVs** (with Dr. Anat Globerson Levin)
- **MSC Placental** EVs for:
  - ✓ cGVHD (with Prof. Ron Ram)
  - ✓ Lung fibrosis (with Dr. Rami Unterman)
  - ✓ Short bowl & Ischemic bowel disease (with Prof. Igor Sukhotnik & Dr. Yoav Ben Shahar)

What questions still needs to be answered, what is needed in order to answer them?

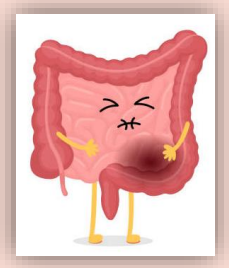
- **EVs as a biomarker** (new projects- collaborations)
- **Explore the effects of EVs on cellular signal transduction**

  (cancer related pregnancy, lung fibrosis, CNS lymphoma)
- **Create modified EVs**

Who we are and our area of interest

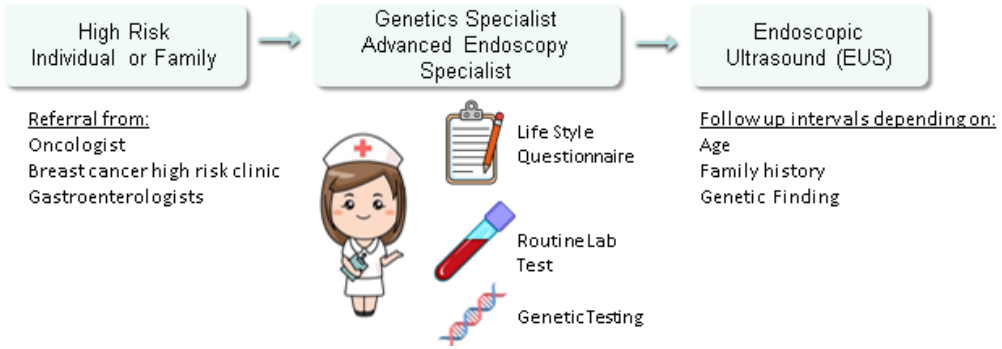
Name of lab/Location	PI/Manager	Main Subjects in the lab	Keep it simple to people who are not in the field
• Gastroenterology clinical lab • Dafna St, third floor	• Merav Ben Yehoyada Ph.D. PI • Guy Rosner M.D. • Reem Abou Research Coordinate	• Early detection of pancreatic cancer (PC) in high risk population. • We explore genetic and post translational modifications as potential markers for early detection of PC. • Biomarker analysis of pancreatic cyst fluids	• Pancreatic cancer has one of the worst prognoses among all malignancies. To date, there are no effective strategies for preventing, diagnosing, or effectively treating this aggressive disease. • High-risk population develop PC at early age • Non-invasive marker development is essential for better treatment and prognosis

Key Capabilities

What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• We established specialized clinic following pancreatic cancer high-risk individuals. we collect data and biological samples to generate comprehensive database	• RT-PCR • NGS • Methylation analysis	• If you need Gasto tests we are here for you…  • Feces handling and analysis (DNA; Protein and soon fat)

What questions still needs to be answered, what is needed in order to answer them?

- In order to explore new early stage PC biomarker, we need to enlarge our cohort. for this purpose, we need other departments / Clinics in the hospital to refer high-risk individuals that meet research criteria to us.



Risk Group
Known genetic mutations carriers (BRCA1, BRCA2, PALB2, ATM CDKN2A, STK11, PRSS1)
Individuals with pancreatic cancer in 1 or 2 first-degree relatives
Individuals with pancreatic cancer in 2 or 3 second-degree relatives
Individuals with pancreatic cancer under the age of 50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MEDICAL CENTER
The Head and Neck Cancer Research Laboratory
Tel-Aviv Sourasky Medical Center
affiliated to Tel Aviv University
Ichilov Scientific Ecosystem

The Head & Neck Cancer Research Lab

Name of lab/Location	• Sami Ofer building, Tel Aviv Medical Center
PI/Manager	• Prof. Nidal Muhanna (MD- PhD) • Lab manager- Dor Rafael (PhD)

The Head & Neck Cancer Research Lab

Main Subjects in the lab

- Targeted nanoparticles for the delivery of siRNA-based therapeutics for head and neck cancer
- The role of cancer associated fibroblasts in the micro-environmet of head and neck cancer
- Immunomodulatory therapeutic strategies for head and neck cancer therapy
- Circulating tumour DNA as a biomarker for diagnosis and surveillance of head and neck cancer patients
- Assessment of effects of anaesthetics and analgesics exposure on serum exosomes and immune responses

Keep it simple to people who are not in the field

- Examining and characterizing cancer- cells and cancer environment for head and neck cancer diagnosis and therapy

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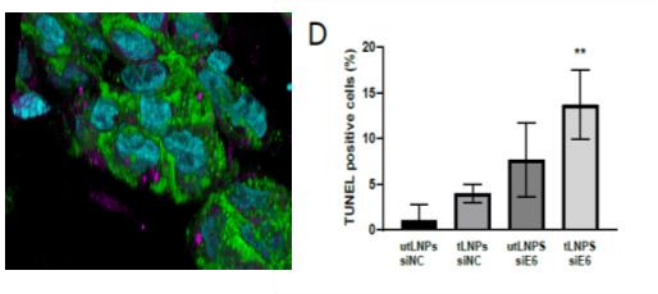
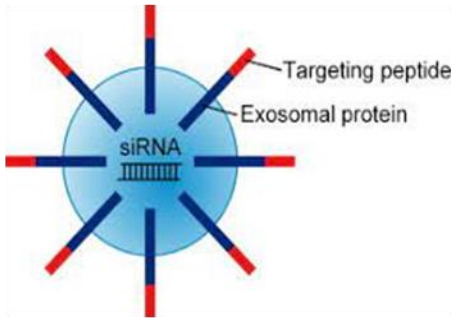
Head and Neck cancer research lab

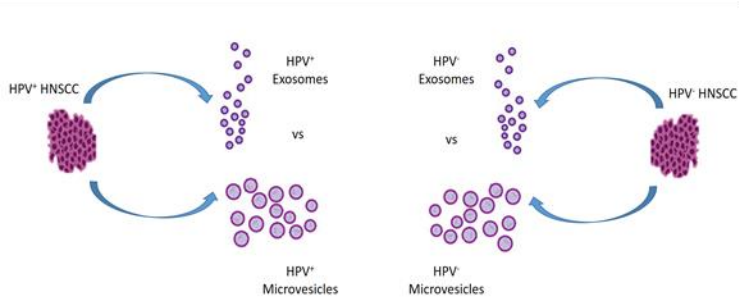
Lipid-based nanpoparticles (LNPs) as siRNA delivery system



Exosomes as endogenous siRNA delivery system

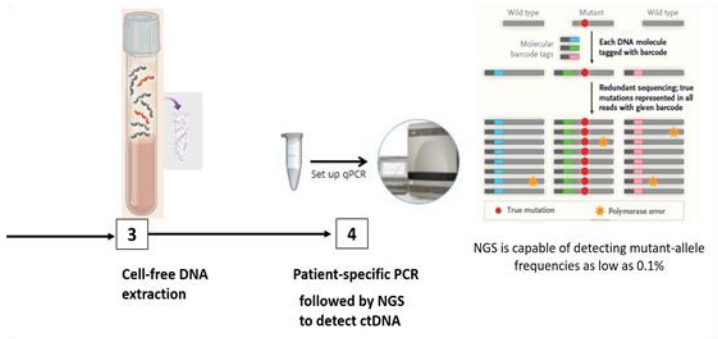


HPV+/HPV- extracellular vesicles and tumor microenvironment



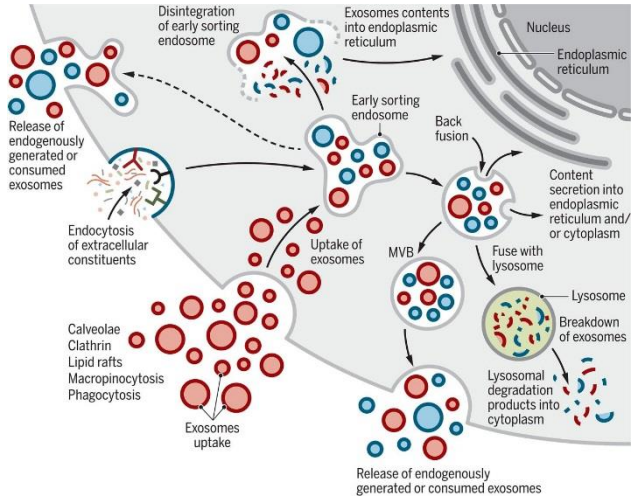
Development of HNSCC Mice model

Ct- detection in liquid biopsy

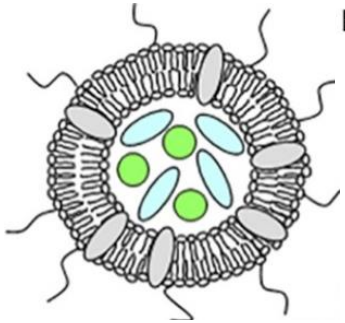


Clinical applications of nanoparticles

Diagnostic



Theranostic

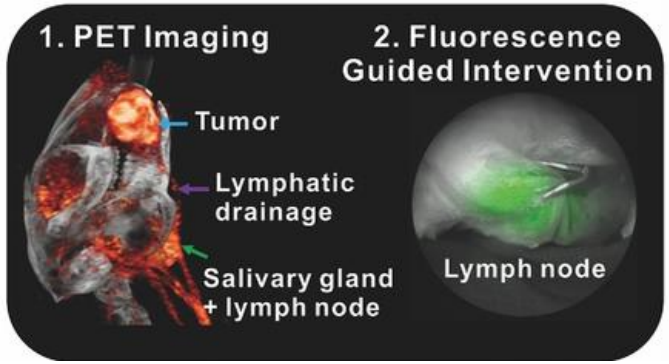


Fluorescence Contrast

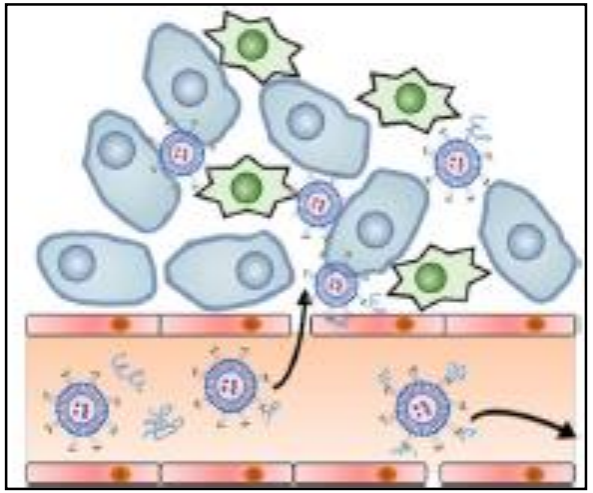
ICG

Iohexol

CT Contrast



Therapeutic



Key Capabilities

What are we specialized in	• Nanoparticles & Tumor micro- environment • Exosomes isolation & characterization • Wound healing
What specialized equipment we use to answer Q	Ultracentrifuge, iBlot, Qubit, PCR, IHC staining, Florescent assays, patient sampling and processing (blood/tissue), In- Vivo models
How can we aid other scientists to answer their Q	Sharing our knowledge in: • Nanoparticles & Exosomes isolation • siRNA • Tumor micro- environment and Biomarkers • ELISA • Immune- response assays- PBMCS purification methods • Lentivirus transfection assays

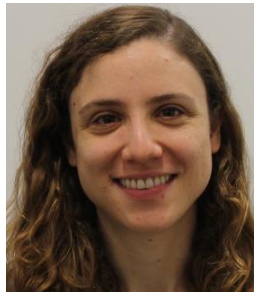
What questions still needs to be answered, what is needed in order to answer them?

- HNSCC tumor cell line establishment → Extract and grow successfully tumor cells from patients
- Tumor spheroids/ tumor organoids formation → Grow HNSCC tumor cell line stably and find efficient protocols for organoids cultures
- Tumor Circulating DNA → Find efficient ways to detect cancer circulating DNA in blood/ saliva samples

Ichilov Scientific Ecosystem

The Team:

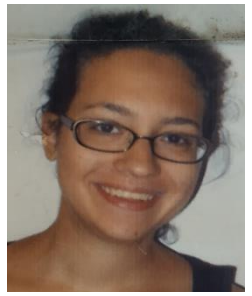

Liyona Kampel
(MD-PhD)


Moran Penn
(MD-PhD)


Yotam Lior
(MD-PhD)


Alexandra Dorman
(MD)


Razan Masarwy
(MD-PhD)


Narin Carmel
(MD)


Dor Rafael (PhD)

Fundings:

הקרן הלאומית למדע
المؤسسة الإسرائيلية للعلوم
Israel Science Foundation

ALROV FUND
קרן אלרוב

"Orion"
physician - scientists
Sponsored by the Kahn Foundation

Collaborators:


Prof. Tal Pupko,
TAU


Prof. Asaf Madi,
TAU

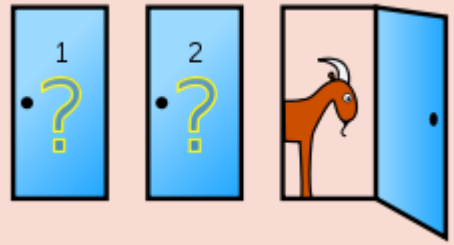

Prof. Dan Peer,
TAU


Prof. Dov Hershkovitz,
TLVMC

Who we are and our area of interest

Name of lab/Location	PI/Manager	Main Subjects in the lab
• Laboratory if the Immuno-HPB and Transplant Surgery • Sammy Ofer building 10th floor room 64-65	• Dr. Shmuel Jaffe Cohen (PI) • Prof. Nir Lubezky (PI)	• Immunology aspects of Hepatobiliary and transplantation surgeries • Gut / liver axis • Liver metastatic niche

Key Capabilities

What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Low biomass Bacterial DNA purification • RT-PCR • Primary cell culture • FACS • Microbiology • In vivo procedures: Liver Surgeries, Gavage, tail-vain injections, perfusion. • In vivo imaging • Preclinical Murine Model of Hepatic Metastases • Microbial EVs • Immunology	• Ultracentrifuge • Nanosight • qRT-PCR • FACS • ELISA • IHC • Confocal microscopy • IVIS • Microbiology facility	Monty Hall problem  MIKIPEDIA

What questions still needs to be answered, what is needed in order to answer them?

- Bioinformatics solutions …
- NGS facility


TLV Biobank
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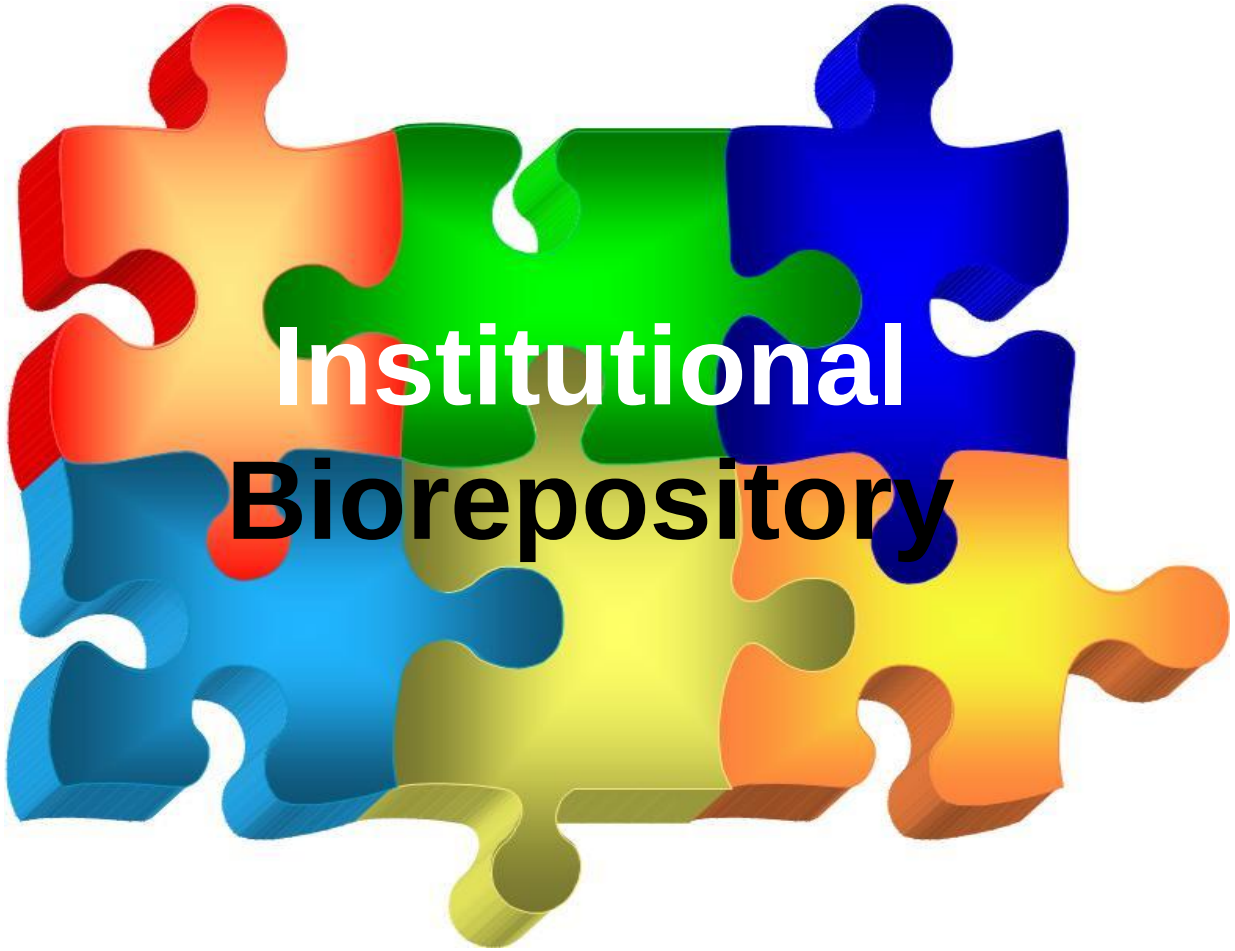
ע"ש סוראסקי
איכילוב

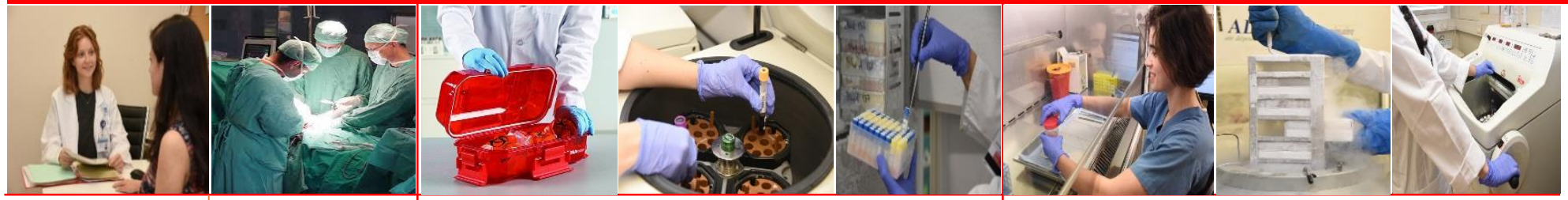

Institutional
Biorepository

Who we are and our area of interest

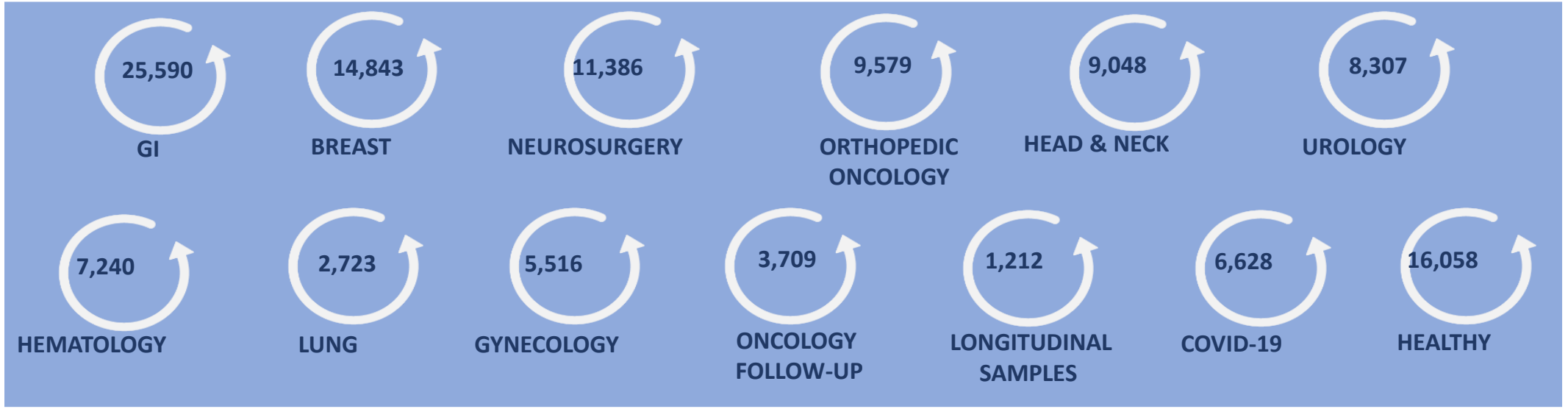
Name of lab/Location	PI/Manager	Main Subjects in the lab	Keep it simple to people who are not in the field
• Pathology lab and BioBank	• Ayelet Itzhaki • Katia Pozyuchenko	• The Institutional Tissue Bank was established to provide the highest quality of biological biospecimens, used as essential tools to achieve the growing demands of the scientific research needs.	• We Collect, process and preserve biosamples

תהליך העבודה ביובנק

Medical Treatment | **Clinical Biobanking** | **Scientific and Medical Research**



Donor Consent* | Medical/ Surgical Procedure | Collection | Processing | Storage | Fresh, Frozen and Fixed Samples

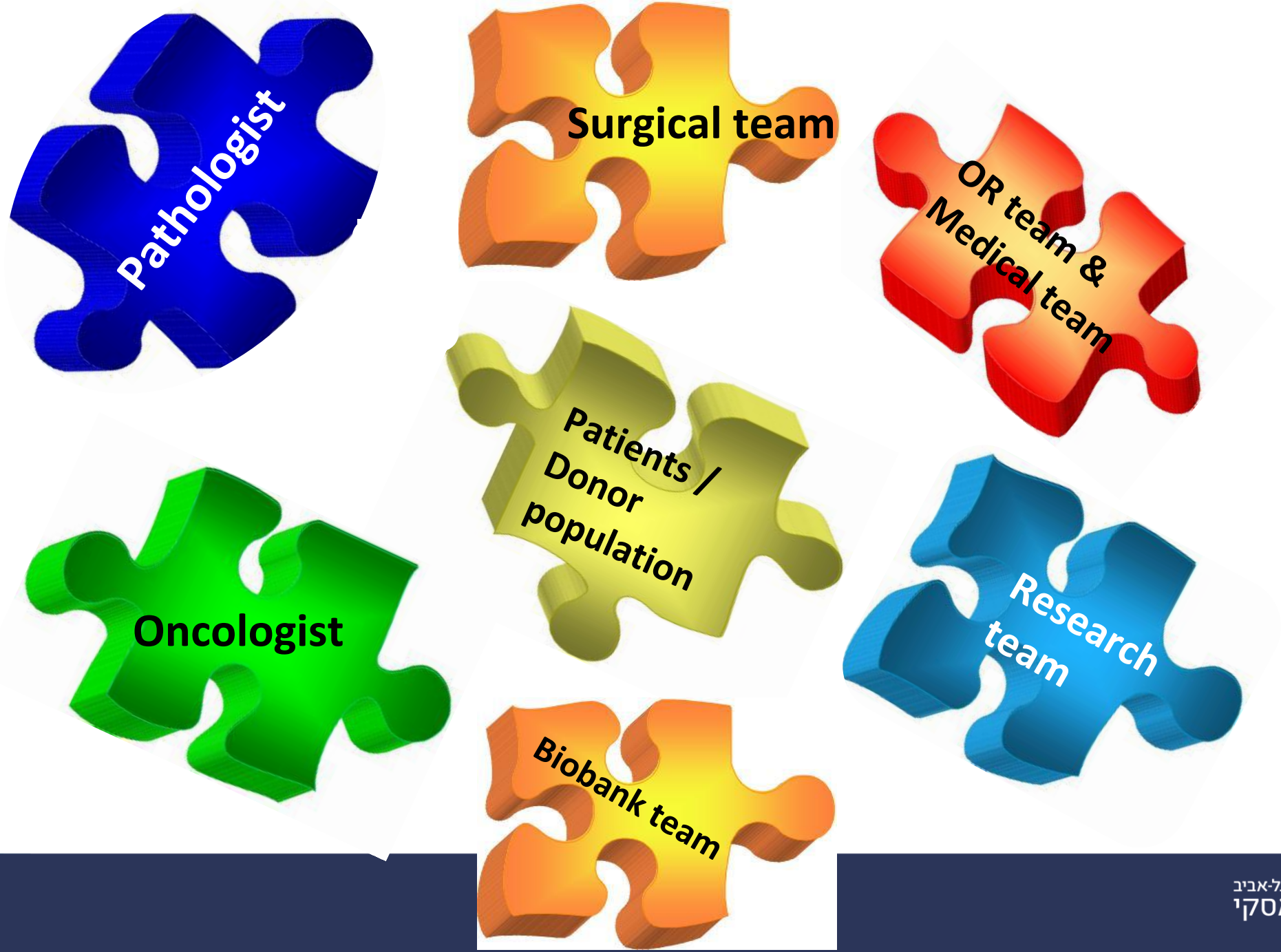


When tissue is not an issue

המרכז הרפואי תל-אביב
ע"ש סוראסקי
איכילוב

What questions still needs to be answered, what is needed in order to answer them?

- The institutional biorepository is working under the regulation of the Ministry Health.
- All donors signed Genomic informed consent form.
- The institutional biorepository is an important and necessary platform for research and will support researchers within and outside the medical center
- Only leftover tissues considered by the pathologist is thought to be bankable.
- All tissues, PBMCs and primary culture samples are kept frozen in liquid nitrogen. Plasma and serum aliquots are stored in -80.
- Medical information of donor samples are documented in the biobank database.
- The samples will be retained as identifiable samples. For investigators, samples can be forwarded in a coded form, unidentifiable form or de-identified manner.
- Clinical information collected: demographic, medical history, surgery report, medication, clinical diagnosis, pathology report & molecular pathology and oncology follow-up.
- Samples processed are according to the CAP regulation and biobanking worldwide SOPs.


Pathologist
Surgical team
OR team &
Medical team
Patients /
Donor
population
Oncologist
Research
team
Biobank team

Who we are and our area of interest

Name of lab/Location	PI/Manager	Main Subjects in the lab
Breast cancer translational research **10th floor rooms 74-76**	Amir Sonnenblik MD PhD Noa-Keren-Khadmy PhD Yael Dogash Almog Becher	• Decipher the mechanisms involved in breast cancer progression and anti-cancer drugs resistance. • The effect of non-oncology drugs • Tumor micro-environment

Key Capabilities

What are we specialized in	What specialized equipment we use to answer Q	How can we aid other scientists to answer their Q
• Human sample collection • qRT-PCR • si/shRNA - viral infection • IP / CoIP (immunoprecipitation) • WB • DNA/RNA extraction from FFPE • Protein structure predication	• Access to clinical databases with genomic analyses • Tissue culture • Pathways inhibitors • Elisa • WB • qRT-PCR • PCR • Breast cancer cell lines	We will be happy to collaborate, think together and to help in any question! ☺

What questions still needs to be answered, what is needed in order to answer them?

- What is the mechanism that enables the treatment resistance?
  - Establish KO cell-line **(Dr. Shifrut)** testing inhibitors effect
- How can we predict the primary tumor response?
  - Research in collaboration with Curesponse and Aummune
- How can we predict relapse?
  - Using digital pathology
- Collaborating with – Ravid Straussman, Neta Erez, Uri Ben-Daviv, Merav Cohen, Ariel Munitz

BIG
Breast International Group

ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology

Duality

TEL AVIV SOURASKY MEDICAL CENTER
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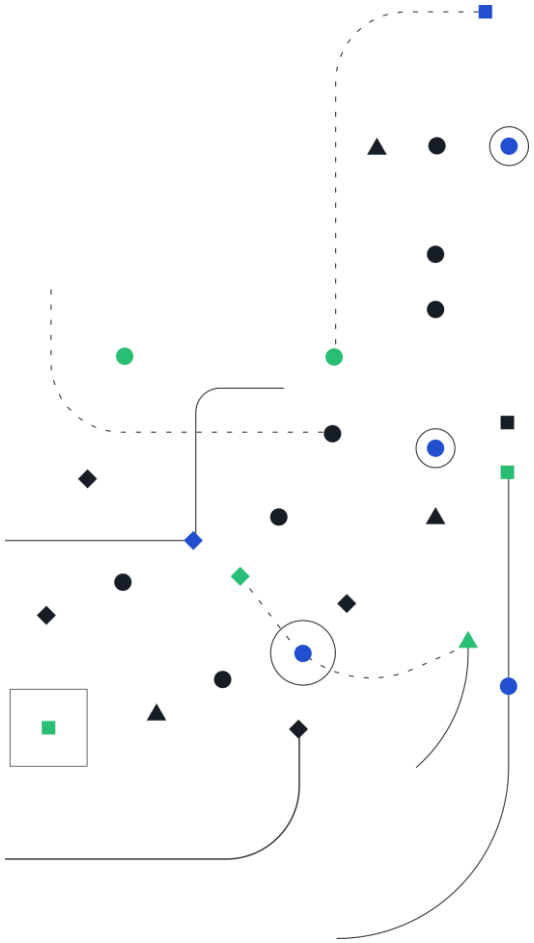


Privacy-Enhanced Analytics on Encrypted Data in Oncology – The path to agile data collaborations

Rina Shainski
Co-founder and Chairwoman
Duality

Dr. Ravit Geva
Head, Research & Innovation Unit
Head, GIT Malignancies Center
Deputy Director Division of Oncology
Tel Aviv Sourasky Medical Center
ICHILOV

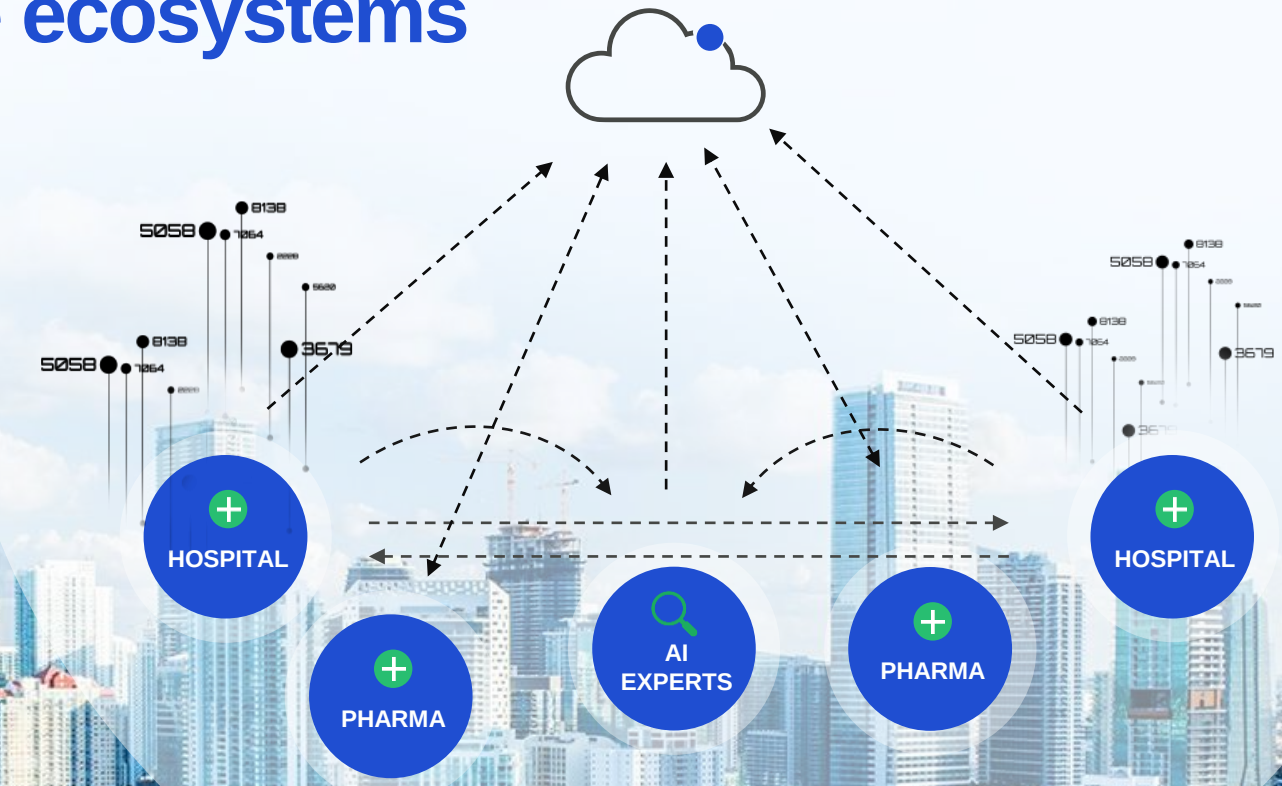
Extracting value from data is necessary for data-driven healthcare ecosystems

1 Enrichment

2 Analysis

3 Collaboration

4 Cloud computing



Duality offers:
Data Science on Encrypted Data!

Security + Privacy + Utility

Powered by quantum-safe **Fully Homomorphic Encryption**
the holy grail of secure computing – **encryption in use**

Driving cancer research in healthcare

NIH National Institute of Mental Health

Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL

TEL AVIV SOURASKY MEDICAL CENTER ICHILOV

Enabling leading medical institutions to **collaborate** and conduct **privacy-enhanced** analysis on **sensitive** data

Privacy Enhanced Multi-Center Data Sharing and Analysis

The Challenge:

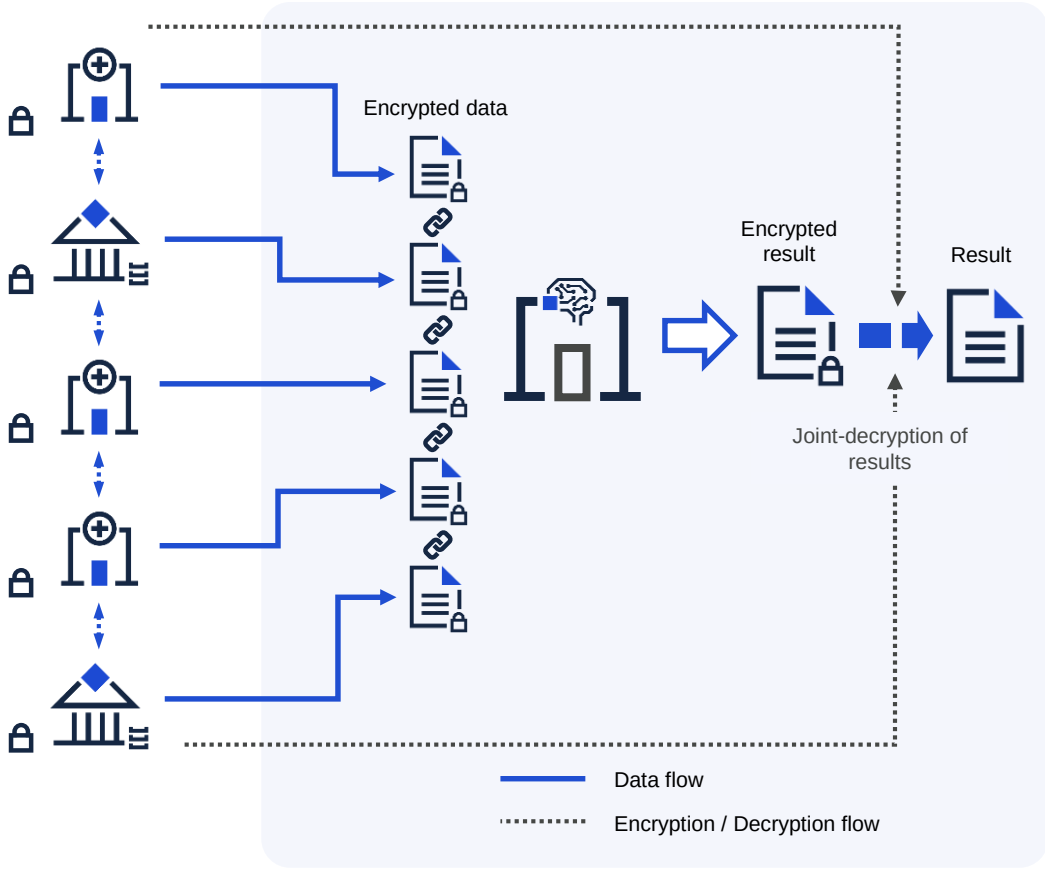
- Patients' data **privacy** – Regulatory constraints
- Researchers want to **control** the use of data

The Solution:

- **Collaborate** on **encrypted** data – security and privacy
- Use neutral environment on encrypted data– CLOUD
- Homomorphic Encryption enables **data-use control**
- Only **analysis results** are decrypted and **shared**

Examples of Analysis:

- Descriptive statistics
- Kaplan-Meier survival analysis
- Fitting regression models
- Correlations and statistical tests
- GWAS and more



Case Study:
Duality and Tel Aviv Sourasky Medical Center

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The Goal

Prove accuracy and practical efficiency of method for real-world evidence studies

The Process

TASMC provided a real-world data set of colorectal cancer patient survival data with 623 patients' records and 24 variables, total 14,952 items of data

The following statistics were calculated on encrypted data (Duality) and plaintext (TASMC):

- Mean
- STD
- Frequencies T-test
- Chi2
- Kaplan-Meier survival analysis
- Logrank of the Kaplan-Meier analysis

The Results

All statistical computations on encrypted data provided the same results as computations with plaintext data

Accuracy of at least 2 decimal digits or more

This opens opportunities for collaborations over sensitive medical data and insights between medical centers and biomedical companies

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Computation		Duality Result	TASMC Results	Run time (Seconds)
Median (Tx_onset_age)		66.005	66	7.32
Mean (Tx_onset_age)		63.52808	63.52808	5.02
Std (Tx_onset_age)		11.73949	11.73949	5.85
Frequencies (Sex)	1	294	294	3.05
	2	329	329	
Chi2 (CannYN / Diagnosis)	chi2	17.9695	17.969	22.77
	p-value	0.021456	0.02146	
Chi2 (CannYN/Sex)	chi2	0.1775	0.1775	11.35
	p-value	0.6735	0.6735	
T-Test (CannYN/Tx_onset_age)	t-score	2.3869	2.387	9.44
	p-value	0.01729	0.01729	
Logrank (CannYN)*	chi2	24.78	24.8	192.26
	p-value	6. 42E-07	6.42E-07	

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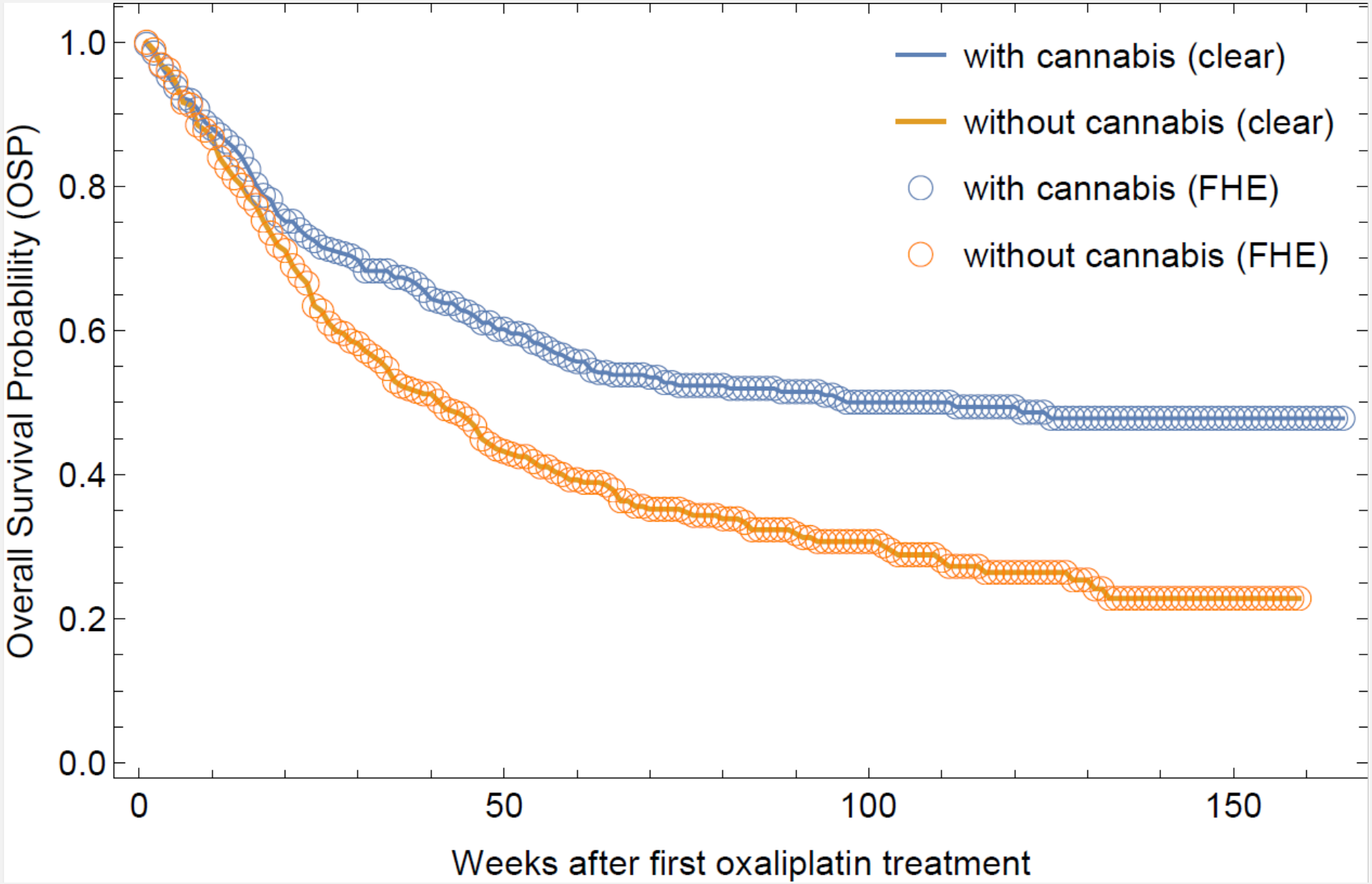

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Confirmatory analysis on previously published data set based on two clinical trials of immunotherapy in renal cell carcinoma

Relative errors for descriptive statistics and survival analysis, - accuracy of more than 5 decimal digits

For frequency computations - the error was zero

FHE Scheme	Computation	Statistic	Rel Error
CKKS	mean	average	2.83e-12
	standard deviation	std dev	1.62e-07
	median	quantile	0.0e+00
	t-test 1	t-score	1.57e-09
	t-test 2	t-score	1.60e-09
	χ^2	χ^2	1.91e-09
	Kaplan-Meier 1	probability	2.04e-07
	Kaplan-Meier 2	probability	7.39e-06
	Kaplan-Meier 3	probability	2.08e-07
	log-rank 1	χ^2	3.21e-08
	log-rank 2	χ^2	4.92e-08
	log-rank 3	χ^2	3.80e-08
BFV	frequency 1	count	0.0e+00
	frequency 2	count	0.0e+00
	frequency 3	count	0.0e+00
	frequency 4	count	0.0e+00

Geva el al in submission to PNAS

Duality

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Thank You