(h	Department of Clinical Microbiology and Immunology Newsletter	Editor Nir Osherov nosherov@post.tau.ac.il	
		Issue 3 1.2.2016	
Our department members at the Zichron Retreat 2015			
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in our department fo	re to share with you all the 4th departmental newsletter. It covers the events r the entire year of 2016.	How my paper was born- interview with	8
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Another new section features two interviews, one with Dr. Dor Salomon, as our newest faculty mem- ber and the second with Prof. Rina Arbesfeld about her recent paper on diseased mummies pub- lished in PLoS One.		departmental face- book page from 2015 Highlights from our	10
	am very proud to mention that our department has been extremely productive scientifically, pub- ishing over 55 papers in excellent journals.		
	rtmental retreat in Zichron, which was also attended by many outgoing mem-	Highlights from our dept retreat Zichron 2017	11
to kind remind you th	I wish you all a happy new 2017 and good luck in your academic work, and just at I am here to help and work with you and my success of serving the depart- is based on teamwork with you.	Picture of the Year	12
Please send me by em and I will help.	ail any comments, suggestions and ideas for things that you want to initiate		
Yours Fuad A. Iraqi Head of Department			

Updates from Our Labs

Dept Head Prof. Fuad Iraqi and Mrs. Esther Flescher at our departmental retreat before awarding of the Flescher Travel Awards



Ph.D student Roa'a Shekh Yousif (Iraqi Lab) giving her talk at our 2016 Zichron retreat.

Motti Gerlic Lab

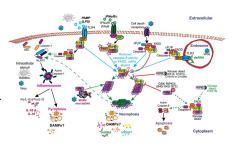
1. Personal Announcements-

Ziv Erlich, PhD student joined the lab

2. Academic announcements- new publications, grants etc.

-Dr. Motti Gerlic was awarded the Recanati grant, Alpha-1 Foundation grant and the Varda and Boaz Dotan Research Center grant

-The Lab of Dr. Motti Gerlic has published:



1: Shlomovitz I, Zargrian S, **Gerlic M**. Mechanisms of RIPK3-induced inflammation. Immunol Cell Biol. 2017 Jan 3. [Epub ahead of print] Review.

2: Murphy AJ, Kraakman MJ, Kammoun HL, Dragoljevic D, Lee MK, Lawlor KE, Wentworth JM, Vasanthakumar A, Gerlic M, Whitehead LW, DiRago L, Cengia L, Lane RM, Metcalf D, Vince JE, Harrison LC, Kallies A, Kile BT, Croker BA, Febbraio MA, Masters SL. IL-18 Production from the NLRP1 Inflammasome Prevents Obesity and Metabolic Syndrome. Cell Metab. 2016 Jan 12:23(1):155-64.

Gal Mor Lab

1. **Personal Announcements**- Alina Goren has received the academic posting of M.Sc. Gili Aviv attended the Gordon Research Conference on Microbial Toxins & Pathogenicity Waterville Valley, NH USA July 10-15, 2016.

2. Academic announcements- new publications, grants etc.

The Gal-Mor Lab has published:

1: Shomer I, Avisar A, Desai P, Azriel S, Smollan G, Belausov N, Keller N, Glikman D, Maor Y, Peretz A, McClelland M, Rahav G, **Gal-Mor O**. Genetic and Phenotypic Characterization of a Salmonella enterica serovar Enteritidis Emerging Strain with Superior Intra-macrophage Replication Phenotype. Front Microbiol. 2016 Sep 16;7:1468.

2: Aviv G, Rahav G, **Gal-Mor O**. Horizontal Transfer of the Salmonella enterica Serovar Infantis Resistance and Virulence Plasmid pESI to the Gut Microbiota of Warm-Blooded Hosts. MBio. 2016 Sep 6;7(5).

3: Baker KS, Dallman TJ, Behar A, Weill FX, Gouali M, Sobel J, Fookes M, Valinsky L, **Gal-Mor O**, Connor TR, Nissan I, Bertrand S, Parkhill J, Jenkins C, Cohen D, Thomson NR. Travel- and Community-Based Transmission of Multidrug-Resistant Shigella sonnei Lineage among International Orthodox Jewish Communities. Emerg Infect Dis. 2016 Sep;22(9):1545-53.

5: Marzel A, Desai PT, Goren A, Schorr YI, Nissan I, Porwollik S, Valinsky L, McClelland M, Rahav G, **Gal-Mor O**. Persistent Infections by NontyphoidalSalmonella in Humans: Epidemiology and Genetics. Clin Infect Dis. 2016 1;62(7):879-86.

6: Elhadad D, Desai P, Grassl GA, McClelland M, Rahav G, **Gal-Mor O**. Differences in Host Cell Invasion and Salmonella Pathogenicity Island 1 Expression between Salmonella enterica Serovar Paratyphi A and Nontyphoidal S. Typhimurium. Infect Immun. 2016 Mar 24;84(4):1150-65.

Ella Sklan Lab

Academic announcements- new publications, grants etc.

1: Levy G, Habib N, Guzzardi MA, Kitsberg D, Bomze D, Ezra E, Uygun BE, Uygun K, Trippler M, Schlaak JF, Shibolet O, **Sklan EH**, Cohen M, Timm J, Friedman N, Nahmias Y. Nuclear receptors control pro-viral and antiviral metabolic responses to hepatitis C virus infection. Nat Chem Biol. 2016 Dec;12(12):1037-1045.

2: Feldman M, Hershkovitz I, **Sklan EH**, Kahila Bar-Gal G, Pap I, Szikossy I, Rosin-Arbesfeld R. Detection of a Tumor Suppressor Gene Variant Predisposing to Colorectal Cancer in an 18th Century Hungarian Mummy. PLoS One. 2016 Feb

New team members, prizes, conferences attended

Udi Qimron Lab.

1. Personal Announcements-

Moran Goren submitted her PhD thesis, and continues research in the lab as a research fellow.

Rea Globus Joined the lab as a Ph.D student.

2. Academic announcements- new publications, grants etc.

-Prof. Qimron was awarded the Sackler Faculty of Medicine Promoting Excellence Award 2016

-The Lab of Prof. Qimron has published :

1: Yosef I, Edgar R, **Qimron U**. Phenotypic heterogeneity in a bacteriophage population only appears as stress-induced mutagenesis. Curr Genet. 2016Nov;62(4):771-773. Review.

2: Goren MG, Doron S, Globus R, Amitai G, Sorek R, Qimron U. Repeat Size Determination by Two Molecular Rulers in the Type I-E CRISPR Array. Cell Rep.2016 Sep 13;16(11):2811-8.

3: Yosef I, Edgar R, Levy A, Amitai G, Sorek R, Munitz A, **Qimron U**. Natural selection underlies apparent stress-induced mutagenesis in a bacteriophage infection model. Nat Microbiol. 2016 Apr 18;1(6):16047.

4: Sternberg SH, Richter H, Charpentier E, Qimron U. Adaptation in CRISPR-Cas Systems. Mol Cell. 2016 Mar 17;61(6):797-808. Review.

5: Yosef I, Manor M, Qimron U. Counteracting selection for antibiotic-resistant bacteria. Bacteriophage. 2016 Mar 7;6(1):e1096996

Fuad Iraqi Lab-

1. Personal Announcements-New students Mrs. Fatma Sarsour -MSc. student

Mrs Rajasree Konar-MSc. Student. Mrs. Hanifa J. Abu-Toamih-Atamni has completed her PhD studies and will start her Postdoctoral position in our lab.

2. Academic announcements- new publications, grants etc.

Prof. Iraqi was awarded the following grants: Binational Science Foundation (BSF) 2016 And the Infrafrontier Horizon 2020 Grant (2016).



Publications 2016:

1: Atamni HJ, Botzman M, Mott R, Gat-Viks I, Iraqi FA. Mapping liver fat female-dependent quantitative trait loci in collaborative cross mice. Mamm

Genome. 2016 Dec;27(11-12):565-573.

2: Abu-Toamih Atamni HJ, Ziner Y, Mott R, Wolf L, Iraqi FA. Glucose tolerance female-specific QTL mapped in collaborative cross mice. Mamm Genome. 2016 Nov 2.

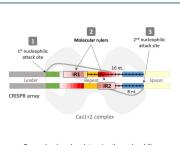
3: Nachshon A, Abu-Toamih Atamni HJ, Steuerman Y, Sheikh-Hamed R, Dorman A, Mott R, Dohm JC, Lehrach H, Sultan M, Shamir R, Sauer S, Himmelbauer H, Iraqi FA, Gat-Viks I. Dissecting the Effect of Genetic Variation on the Hepatic Expression of Drug Disposition Genes across the Collaborative Cross Mouse Strains. Front Genet. 2016 Oct 5;7:172.

4: De Simone M, Spagnuolo L, Lorè NI, Cigana C, De Fino I, Broman KW, **Iraqi FA**, Bragonzi A. Mapping genetic determinants of host susceptibility to Pseudomonas aeruginosa lung infection in mice. BMC Genomics. 2016 May 11;17:351.

5: Dorman A, Baer D, Tomlinson I, Mott R, Iraqi FA. Genetic analysis of intestinal polyp development in Collaborative Cross mice carrying the Apc (Min/+) mutation. BMC Genet. 2016 Feb 19;17:46.

6: Atamni HJ, Mott R, Soller M, Iraqi FA. High-fat-diet induced development of increased fasting glucose levels and impaired response to intraperitoneal glucosechallenge in the collaborative cross mouse genetic reference population. BMC Genet. 2016 Jan 5;17:10.

7. Nashef A, Egbaria M, Shusterman A, Lore N, Bragonzi A, Wiess E, Houri-Haddad Y and **Fuad FA** (2016) Dissection of host susceptibility to Bacterial infections and its toxins. System Genetics: Methods and Protocols. Editors Kalus Schughart and Robert Williams. To be published by Springer Science + Business Media, LLC, New York.



Two molecular rulers determine the nucleophilic attack site at the leader-distal repeat-end 3



Yona Keisari Lab

1. Personal Announcements

Adi Cohen Joined the lab as an M.Sc. Student. Clinical Trials with alpha DaRT, our alpha radiation based cancer treatment, will start at the end of January 2017 in Rabin Medical Center.

2. Academic announcements- new publications, grants etc.

-The Lab of Prof. Yona Keisari has published:

1: Confino H, Schmidt M, Efrati M, Hochman I, Umansky V, Kelson I, **Keisari Y**. Inhibition of mouse breast adenocarcinoma growth by ablation with intratumoral alpha-irradiation combined with inhibitors of immunosuppression and CpG. Cancer Immunol Immunother. 2016 Oct;65(10):1149-58.

4: Keisari Y. Tumor abolition and antitumor immunostimulation by physico-chemical tumor ablation. Frontiers Biosc. (Landmark edition), 22: 310-347, 2017.

Rina Arbesfeld Lab

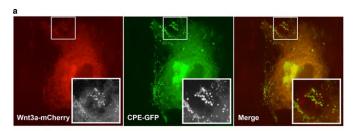
New publications, grants etc.

1: Yedid N, Kalma Y, Malcov M, Amit A, Kariv R, Caspi M,

Rosin-Arbesfeld R, Ben-Yosef D. The effect of a germline

mutation in the APC gene on $\boldsymbol{\beta}\text{-catenin}$ in human embryonic

stem cells. BMC Cancer. 2016 Dec 23;16(1):952.



2: Skalka N, Caspi M, Lahav-Ariel L, Loh YP, Hirschberg K, Rosin-Arbesfeld R. Carboxypeptidase E (CPE) inhibits the secretion and activity of Wnt3a. Oncogene. 2016 Dec 15;35(50):6416-6428.

3: Kuslansky Υ, Sominsky S, Jackman A, Gamell C, Monahan BJ, Haupt Υ, Rosin-Arbesfeld R, Sherman L. Ubiquitin ligase E6AP mediates nonproteolytic polyubiquitylation of β-catenin independent of the E6 oncoprotein. J Gen Virol. 2016 Dec;97(12):3313-3330.

4: Caspi M, Firsow A, Rajkumar R, Skalka N, Moshkovitz I, Munitz A, Pasmanik-Chor M, Greif H, Megido D, Kariv R, Rosenberg DW, **Rosin-Arbesfeld R**. A flow cytometry-based reporter assay identifies macrolide antibiotics as nonsense mutation read-through agents. J Mol Med (Berl). 2016 Apr;94 (4):469-82.

5: Feldman M, Hershkovitz I, Sklan EH, Kahila Bar-Gal G, Pap I, Szikossy I, Rosin-Arbesfeld R. Detection of a Tumor Suppressor Gene Variant Predisposing to Colorectal Cancer in an 18th Century Hungarian Mummy. PLoS One. 2016 Feb 10;11(2):e0147217.

Ilan Tsarfaty Lab

Academic announcements- new publications, grants etc.

1: Bar-Lev Y, Moshitch-Moshkovitz S, Tsarfaty G, Kaufman D, Horev J, Resau JH, **Tsarfaty I**. Mimp/Mtch2, an Obesity Susceptibility Gene, Induces Alteration of Fatty Acid Metabolism in Transgenic Mice. PLoS One. 2016 Jun 30;11(6):e0157850.

Ariel Munitz Lab

Personal announcements-Inbal Mudahi- MSc student, Esther Schnayderman- MSc student, Shulik Avlas- MSc student

Academic announcements- new publications, grants etc.

Patents: Antibodies to Interleukin 13 receptor alpha and uses thereof. US Provisional Patent Application 62/330,276; 2016

1: Elhaik Goldman S, Moshkovits I, Shemesh A, Filiba A, Tsirulsky Y, Vronov E, Shagan M, Apte RN, Benharroch DA, Karo-Atar D, Dagan R, Munitz A, Mizrachi Nebenzahl Y, Porgador A. Natural Killer Receptor 1 Dampens the Development of Allergic Eosinophilic Airway Inflammation. PLoS One. 2016 Aug 31;11(8):e0160779.

2: Ben Baruch-Morgenstern N, Mingler MK, Stucke E, Besse JA, Wen T, Reichman H, **Munitz A**, Rothenberg ME. Paired Ig-like Receptor B Inhibits IL -13-Driven Eosinophil Accumulation and Activation in the Esophagus. J Immunol. 2016 Aug 1;197(3):707-14.

3: Munitz A, Karo-Atar D, Foster PS. Asthma diagnosis: MicroRNAs to the rescue. J Allergy Clin Immunol. 2016 May;137(5):1447-8. Review.

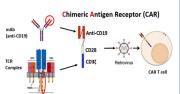
4: Moshkovits I, Reichman H, Karo-Atar D, Rozenberg P, Zigmond E, Haberman Y, Ben Baruch-Morgenstern N, Lampinen M, Carlson M, Itan M, Denson LA, Varol C, Munitz A. A key requirement for CD300f in innate immune responses of eosinophils in colitis. Mucosal Immunol. 2016 Apr 27.

5: Yosef I, Edgar R, Levy A, Amitai G, Sorek R, Munitz A, Qimron U. Natural selection underlies apparent stress-induced mutagenesis in a bacteriophage infection model. Nat Microbiol. 2016 Apr 18;1(6) infection model. Nat Microbiol. 2016 Apr 18;1(6):16047.

Michal Besser Lab

Personal Announcements- Sivan Ofir has join the lab as MSc student. Meir Rozenbaum and Hadas Weinstein -Marom have joined as post-doc students. Michal Levy has joined as technician. Naama Dror has left the lab. **Academic announcements**- new publications, grants etc. The lab of Michal Besser was awarded the Dotan

Center in Hemato-Oncology Grant. The lab received the approval of the Ministry of Health to produce T cells genetically modified to express a Chimeric Antigen Receptor (CAR) against CD19 for the treatment of pediatric patients and adults with B



cell malignancies (see Figure). 1: Ben-Avi R, Itzhaki O, Simansky D, Zippel D, Markel G, Ben Nun A, Schachter J, **Besser MJ**. Metastatic Lung Lesions as a Preferred Resection Site forImmunotherapy With Tumor Infiltrating Lymphocytes. J Immunother. 2016 Jun;39(5):218-22

2: Marcu-Malina V, Garelick D, Peshes-Yeloz N, Wohl A, Zach L, Nagar M, Amariglio N, **Besser MJ**, Cohen ZR, Bank I. Peripheral blood-derived, γ9δ2 t cell-enriched cell lines from glioblastoma multiforme patients exert anti-tumoral effects in vitro. J Biol Regul Homeost Agents. 2016 Jan-Mar;30(1):17-30.

3: Weinstein-Marom H, Pato A, Levin N, Susid K, Itzhaki O, **Besser MJ**, Peretz T, Margalit A, Lotem M, Gross G. Membrane-attached Cytokines Expressed by mRNA Electroporation Act as Potent T-Cell Adjuvants. J Immunother. 2016 Feb-Mar;39(2):60-70.

4: Kalaora S, Barnea E, Merhavi-Shoham E, Qutob N, Teer JK, Shimony N, Schachter J, Rosenberg SA, **Besser MJ**, Admon A, Samuels Y. Use of HLA peptidomics and whole exome sequencing to identify human immunogenic neo-antigens. Oncotarget. 2016 Feb 2;7(5):5110-7.

5: Fellerhoff-Losch B, Korol SV, Ganor Y, Gu S, Cooper I, Eilam R, Besser M, Goldfinger M, Chowers Y, Wank R, Birnir B, Levite M. Normal human CD4+ helper T cells express Kv1.1 voltage-gated K+ channels, and selective Kv1.1 block in T cells induces by itself robust TNFa production and secretion and activation of the NFkB non-canonical pathway. J Neural Transm (Vienna). 2016 123(3):137-57

6: Markel G, Imazio M, Koren-Morag N, Galore-Haskel G, Schachter J, Besser M, Cumetti D, Maestroni S, Altman A, Shoenfeld Y, Brucato A, Adler Y. CEACAM1 and MICA as novel serum biomarkers in patients with acute and recurrent pericarditis. Oncotarget. 2016 Apr 5;7(14):17885-95. doi: 10.18632/oncotarget.7530.

7: Ashkenazi S, Ortenberg R, Besser M, Schachter J, Markel G. SOX9 indirectly regulates CEACAM1 expression and immune resistance in melanoma cells. Oncotarget. 2016 May 24;7(21):30166-77.

8: Zikich D, Schachter J, Besser MB. Predictive markers of TIL efficiency. Immunother. 2016 8(1):35-43. (Review)

Nir Osherov Lab

1. Personal Announcements-

-Dafna Ben Yaakov has left our lab and is writing up her PhD. Thesis.

- Adi Perevitsky has left our lab and is writing up his M.Sc. Thesis.

2. Academic announcements-

Patents- Benhar I, Osherov N, Dergachev V, Szpilman (2016). Amphotericin B derivatives.

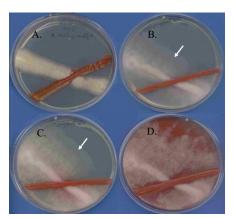
1: Osherov N, Kontoyiannis DP. The anti-Aspergillus drug pipeline:

Is the glass half full or empty? Med Mycol. 2017 Jan 1;55(1):118-124.

2: Vitenshtein A, Charpak-Amikam Y, Yamin R, Bauman Y, Isaacson B,

Stein N, Berhani O, Dassa L, Gamliel M, Gur C, Glasner A, Gomez C,

Ben-Ami R, Osherov N, Cormack BP, Mandelboim O. NK Cell Recognition



of Candida glabrata through Binding of NKp46 and NCR1 to Fungal Ligands Epa1, Epa6, and Epa7. Cell Host Microbe. 2016 Oct 12;20(4):527-534.

3: Kaltdorf M, Srivastava M, Gupta SK, Liang C, Binder J, Dietl AM, Meir Z, Haas H, **Osherov N**, Krappmann S, Dandekar T. Systematic Identification of Anti-Fungal Drug Targets by a Metabolic Network Approach. Front Mol Biosci. 2016 Jun 17;3:22.

4: Vaknin Y, Hillmann F, Iannitti R, Ben Baruch N, Sandovsky-Losica H, Shadkchan Y, Romani L, Brakhage A, Kniemeyer O, **Osherov N**. Identification andCharacterization of a Novel Aspergillus fumigatus Rhomboid Family Putative Protease, RbdA, Involved in Hypoxia Sensing and Virulence. Infect Immun. 2016 May 24;84(6):1866-78.

5: Hover T, Maya T, Ron S, Sandovsky H, Shadkchan Y, Kijner N, Mitiagin Y, Fichtman B, Harel A, Shanks RM, Bruna RE, García-Véscovi E, **Osherov** N. Mechanisms of Bacterial (Serratia marcescens) Attachment to, Migration along, and Killing of Fungal Hyphae. Appl Environ Microbiol. 2016 Apr 18;82(9):2585-94.

6: Osherov N, Ben-Ami R. Modulation of Host Angiogenesis as a Microbial Survival Strategy and Therapeutic Target. PLoS Pathog. 2016 Apr 14;12 (4):e1005479. doi:10.1371/journal.ppat.1005479. Review.

7: Ben Yaakov D, Rivkin A, Mircus G, Albert N, Dietl AM, Kovalerchick D, Carmeli S, Haas H, Kontoyiannis DP, **Osherov N**. Identification and characterization of haemofungin, a novel antifungal compound that inhibits the final step of haem biosynthesis. J Antimicrob Chemother. 2016 Apr;71 (4):946-52.

8: Halperin A, Shadkchan Y, Pisarevsky E, Szpilman AM, Sandovsky H, Osherov N, Benhar I. Novel Water-Soluble Amphotericin B-PEG Conjugates with Low Toxicity and Potent in Vivo Efficacy. J Med Chem. 2016 Feb 11;59(3):1197-206.

Gal Markel Lab

1. Personal Announcements- Shira Ashkenazi's PhD was approved

Left the lab in 2016: Dr Eyal Greenberg, Dr Gilli Galor, Karin Kfir

Joined the lab in 2016: Dr Ettai Markovitch, Dr Erez Baruch

Gal Markel was awarded a Kamin grant in collaboration with Prof Tami Geiger

2. Academic announcements- new publications, grants etc.

1: Vitenshtein A, Weisblum Y, Hauka S, Halenius A, Oiknine-Djian E, Tsukerman P, Bauman Y, Bar-On Y, Stern-Ginossar N, Enk J, Ortenberg R, Tai J, **Markel G**, Blumberg RS, Hengel H, Jonjic S, Wolf DG, Adler H, Kammerer R, Mandelboim O. CEACAM1-Mediated Inhibition of Virus Production. Cell Rep. 2016 Jun 14;15(11):2331-9.

2: Harats M, Millet E, Jaeger M, Orenstein A, Haik J, Hajdu SD, **Markel G**, Winkler E, Tessone A. Adipocytes Viability After Suction-Assisted Lipoplasty: Does the Technique Matter? Aesthetic Plast Surg. 2016 Aug;40(4):578-83.

3: Ben-Avi R, Itzhaki O, Simansky D, Zippel D, **Markel G**, Ben Nun A, Schachter J, Besser MJ. Metastatic Lung Lesions as a Preferred Resection Site for Immunotherapy With Tumor Infiltrating Lymphocytes. J Immunother. 2016 Jun;39(5):218-22.

4: Markel G, Imazio M, Koren-Morag N, Galore-Haskel G, Schachter J, Besser M, Cumetti D, Maestroni S, Altman A, Shoenfeld Y, Brucato A, Adler Y. CEACAM1 and MICA as novel serum biomarkers in patients with acute and recurrent pericarditis. Oncotarget. 2016 Apr 5;7 (14):17885-95. doi: 10.18632/oncotarget.7530.

5: Ashkenazi S, Ortenberg R, Besser M, Schachter J, **Markel G**. SOX9 indirectly regulates CEACAM1 expression and immune resistance in melanoma cells. Oncotarget. 2016 May 24:7(21):30166-77.

6: Haik J, Nardini G, Goldman N, Galore-Haskel G, Harats M, Zilinsky I, Weissman O, Schachter J, Winkler E, **Markel G**. Increased serum NKG2D-ligands and downregulation of NKG2D in peripheral blood NK cells of patients with major burns. Oncotarget. 2016 Jan 19;7(3):2220-8.

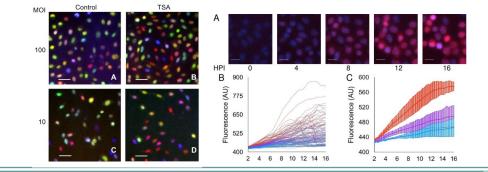
Oren Kobiler Lab

Academic announcements- new publications, grants etc.

1: Shapira L, Ralph M, Tomer E, Cohen S, **Kobiler O**. Histone Deacetylase Inhibitors Reduce the Number of Herpes Simplex Virus-1 Genomes Initiating Expression in Individual Cells. Front Microbiol. 2016 Dec 6;7:1970.

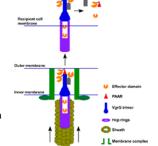
2: Cohen EM, Kobiler O. Gene Expression Correlates with the Number of Herpes Viral Genomes Initiating Infection in Single Cells. PLoS Pathog. 2016 Dec 6;12(12):e1006082.

3: Yamin D, Jones FK, DeVincenzo JP, Gertler S, Kobiler O, Townsend JP, Galvani AP. Vaccination strategies against respiratory syncytial virus. Proc Natl Acad Sci U S A. 2016 Nov 15;113(46):13239-13244.



Dor Salomon Lab

- 1. Personal Announcements
 - Nika Schwartz joined as the new lab manager Adi Karni joined as a M.Sc. student.

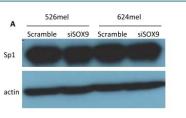


2. Academic Announcements

Dr. Salomon was awarded the Alon Fellowship for young investigators given by the Higher Education Council.

Dr. Salomon was awarded the European Research Council (ERC) starting grant for 5 years.

The Type 6 secretion system



An interview with Dr. Dor Salomon, our new bacteriologist group leader...



Dor and his wife, Laura.



Dor and his new lab group- Nika Schwartz (right) and Adi Karni (center)

Can you give us some personal details if possible- where do you live, your family, kids etc? what activities do you enjoy outside of work? Do you have hobbies?

I've lived all my life in the north of Tel Aviv, close to TAU. After a 5-year post-doc excursion to Dallas, Texas, I came back to the same neighborhood I grew up in. While in Dallas, I met my wife (who was born and raised there) who is now learning Hebrew and working as a web/mobile developer. My wife and I are "foodies", so we like good food and wine (my mother being the author of cooking books doesn't hurt...).

Tell us a bit about your academic journey- where did you study as an undergraduate, your Ph.D-with whom and on what? Your post doc with whom and on what? After your post-doc, where?

I did my undergrad studies at the Faculty of Life Sciences at TAU as part of the Biotechnology Program. During my 3rd year I was working at Prof. Shosh Bar-Nun's lab at the Department of Biochemistry studying the ER-associated protein degradation pathway in yeast. After graduating, I continued at the Faculty of Life Sciences in the Dean's direct Ph.D. track. My first 4 month rotation was done in Prof. Guido Sessa's lab at the Department of Molecular Biology and Ecology of Plants working on plant-pathogen interactions; my second rotation was in Prof. Danni Canaani's lab at the Department of Biochemistry working on breast cancer metastasis. I was intrigued by the arms-race between bacteria and eukaryotic hosts so I decided to join the Sessa lab to complete my Ph.D., where I was studying plant immune responses and bacterial type III secretion system effectors using plant and yeast models. Guido gave me a lot of freedom and support to study what interests me and I am grateful for that as it made me more independent and gave me tools and experience that aided me in my postdoc. I wanted to continue working on bacterial toxins and understand their mechanisms of action, so for my postdoc I joined Prof. Kim Orth's lab at the University of Texas Southwestern Medical Center at Dallas, Texas. I was very fortunate because Kim's philosophy toward postdocs is that each postdoc has two projects: one for the lab and the other for themselves (to take with them when they land a Faculty position). Luckily, both projects were fruitful (studying type III secretion system effectors for the lab, and characterizing the type VI secretion systems for me). When I felt that I was ready, I applied for Faculty positions in Israel and the USA, and here I am.

What is the focus of your research in your lab at Sackler?

We study bacterial secretion systems and toxins, trying to understand their function, targets, and regulation. The system we mainly focus on currently is the type VI secretion system (T6SS). It was only discovered in 2006 and it is unique as, unlike other secretion systems, it can target both eukaryotic and bacterial cells to mediate virulence and antibacterial toxicity. During my postdoc I discovered a widespread class of polymorphic toxins delivered by T6SSs, which carry various toxin domains. Our goal is to understand what these toxins are doing and then use these systems and toxins to engineer novel antibacterial platforms and treatments.

What do you find most interesting in your field? In biology?

I am fascinated by bacteria and how these small "simple" organisms carry so much "knowledge" and ability to shape their world into what they desire. There is just so much to learn about biology from bacterial toxins. They are designed to target specific pathways in eukaryotic cells and we owe a lot of our current cell biology understanding to work done on such bacterial toxins. Now, with the discovery of the antibacterial toxins of the T6SS, we can also use bacterial "knowledge" to find new antibacterial targets and mechanisms to develop drugs. Č

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Lead author Michal Feldman



A mummy from the Hungarian Vac collection

How my paper was born- an interview with Prof. Rina Arbesfeld about her recent paper on Hungarian mummies in PLoS One.

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Title of paper-. "Detection of a Tumor Suppressor Gene Variant Predisposing to Colorectal Cancer in an 18th Century Hungarian Mummy"

Principle investigator- Rina Arbesfeld-Rosin

Lead authors- Michal Feldman

Published in- PLoS One

Question-Tell us about the most important findings in your paper? What are the implications?

We set out to identify mutations in the APC gene that predispose to colorectal cancer in ancient DNA samples of humans preserved from the 18th century in a family burial crypt in a church in Vac Hungary. These mummies are now kept in the Budapest natural History Museum. We also wanted to try and identify together with Dr. Ella Sklan, if any of the mummies were infected with hepatitis viruses but in this we were not successful. Prof Israel Hershkovitch, our collaborator and a world expert in anthropology, operated on 3 mummies. The samples were analyzed by PCR in a special "sterile" lab by student Michal Feldman.

Our most important finding was that we discovered the E1317Q missense mutation, known to be a colorectal cancer predisposing mutation, in a large intestine tissue of one of the three mummies we tested. This result suggests that genetic predisposition to cancer already existed in the pre-industrialization era.

Question- How was the idea for this study born?

Prof. Israel Hershkovitch is my "next door neighbor" in the department and the idea was born out of random chats and conversations we had. We decided to join forces- Israel contributing his passion for anthropology and human prehistory and myself contributing my interest in cancer and Wnt signaling, including the APC gene product which negatively regulates this pathway.

Question- What were the hardest part of the research itself?

The hardest part of the study was in isolating the ancient DNA. The main problem was that it came from soft tissue in the gut, which is not an ideal source like bones and teeth because it decomposes rapidly and contains mainly bacterial DNA. We were lucky in that the mummies were encased in pine wood shavings that helped preserve the DNA and that they were kept in the crypt under relatively dry and ventilated conditions. We were also extremely worried about contaminating the mummy DNA with our own DNA. To make sure we were not sequencing ourselves, we all underwent DNA sequencing using the same primers used on the mummies. Still it was very hard to isolate quality DNA, good enough to PCR amplify. Luckily we knew the exact short DNA regions in which the common APC mutations occur, so we could generate fragments for sequencing even though the DNA we isolated was not very good quality. The happiest part was finding the APC mutation in just one of the three mummies that we were able to get readable DNA from!

We took extreme precautions to avoid contamination of the mummy DNA- The samples were taken using a no-touch technique with disposable scalpels, from inner organs. These anatomical regions were not previously exposed to the outside environment and therefore were protected from contact with excavators or others that have handled the mummies. DNA was extracted in a designated ancient DNA (aDNA) laboratory. To prevent contamination by contemporary DNA the tubes were opened only in a designated UV eradiated hood where DNA extraction was carried out. The aDNA laboratory was physically isolated from the laboratory where modern DNA was used. The procedure was carried out in sterile UV chambers each equipped with separate set of pipettes, disposable sterile tubes, filter tips, molecular biology grade reagents and solutions. Disposable protective clothing was used and changed frequently. Separate UV-irradiated hoods were used for DNA preparation, DNA extractions and PCR

preparation. To further minimize contemporary DNA contamination all reagents, tubes and instruments such as disposable scalpel blades were irradiated with UV prior to use. Multiple negative controls for extraction and amplification were included to ensure the authenticity of the aDNA findings.

Question- What are you planning to do next in this exciting project?

We would really like to continue this line of work, however we lack two important elements- funding and a specialized lab dedicated to analyzing ancient DNA, that needs to be set up here at TAU. Prof. Hershkovitz our collaborator in this project, is working towards this goal.

Interesting things from our departmental Facebook Page-



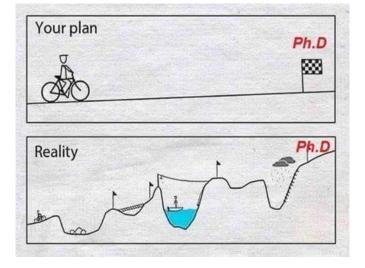
PRODUCT OF INTELLIGENT DESIGN

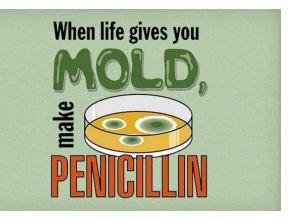












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Prof. Yona Keisari



Prof. Fuad Iraqi, dept head and Dr. Oren Kobiler



Dr Efrat Shoham- Besser Group

Pics from our departmental retreat Zichron 2016

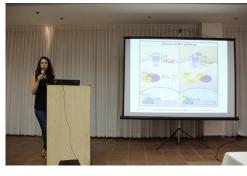


Bella Vizel- Markel group



Perry Rosenberg- Munitz group





Orian Elisha, Arbesfeld group



Osherov group



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Tsarfaty group





Rea Globus- Qimron group



Einav Shemesh- Osherov group



Oren Oster- Qimron group



Dafna receiving Flescher award



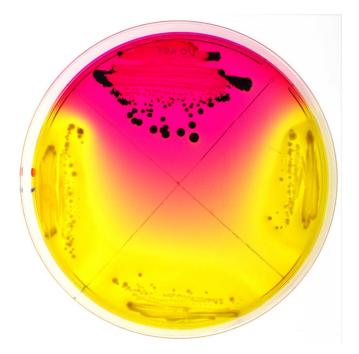


Members of Arbesfeld and Sklan labs



Ronen receiving Flescher award

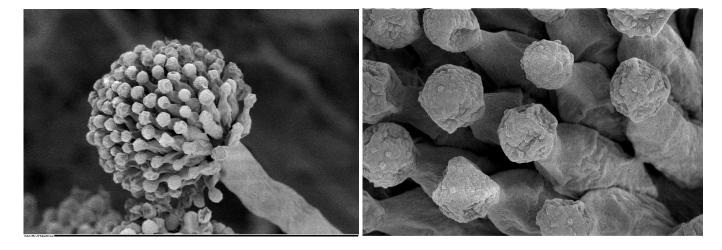
Lab Images of the Year



Ohad Gal-mor Lab: The image shows *Salmonella enterica* serovar Infantis (**black colonies** at the top of the plates).

This is an emerging strain that carries a megaplasmid, encoding many virulence and resistance genes.

When we infected mice with this strain we were able to show that this large virulence plasmid can be transferred to the mouse microbiota. The **yellow colonies** were formed by three independent commensal *E. coli* isolates that have acquired the *Salmonella* megaplasmid during the infection within the mouse.



Osherov Lab: The image shows Aspergillus fumigatus conidiophore (left)

with forming asexual spores (conidia). Right- close-up of conidia and underlying spore producing cells called phialides.

TEM images were taken in collaboration with Prof. Amnon Harel and Dr, Boris Fichtman (BIU).

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