Name:Roi Gazit; ORCID# 0000-0002-0548-2147

Current Position Title: Associate Professor

The Shraga Segal department of Microbiology Immunology and Genetics, Faculty of Health Sciences, Ben-

Gurion University of the Negev, Beer Sheva, Israel

Email Address: gazitroi@bgu.ac.il; lab website https://www.roigazitlab.com/

Education/Training

Institution, City, Country	Degree (if applicable)	Completion Date MM/YYYY	Field of Study
Hebrew University of Jerusalem, Israel	B.Sc.	1997-1999	Biology
Hebrew University of Jerusalem, Israel	M.Sc.	2000-2001	Developmental Biology
Hebrew University of Jerusalem, Israel	Ph.D.	2002-2007	Immunology
Harvard Medical School, Boston, MA, USA	PostDoc	2008-2013	Hematopoietic Stem cell

A. Personal Statement

My laboratory is focusing on the study of hematopoietic stem cells (HSCs) and immunology, with interests into basic biology, and cancer. HSCs are the best studied adult stem cells, already saving thousands of lives every year. Surprisingly, however, little is understood about the molecular mechanisms that enable HSC to sustain multi-potency and self-renewal for life time. Better understanding of HSCs will provide translational opportunities for such needed stem-cells, and shed new light on normal and malignant adult stem cells. Studying HSCs within the immune-system under naïve, immunological stimulated and along aging is aiming to further determine stem cells dynamic activities. We have special interest in Leukemias, which are closely related with stem-cells, and in the study of Multiple-Myeloma to understand clonality and reveal better ways to eradicate malignancy.

B. Positions and Employment

1.2013 –12.2019 Senior Lecturer, the Shraga Segal Department of Microbiology, Immunology, and Genetics; Faculty of Health Sciences, Ben-Gurion University of the Negev

12.2019 - Associate Professor, the Shraga Segal Department of Microbiology, Immunology, and Genetics; Faculty of Health Sciences, Ben-Gurion University of the Negev

Other Experience and Professional Memberships

2020- Current Vice-president and finance of Israel Immunology Society

2020- Current Chair of Ethical Committee for animals at the Ben-Gurion University

2019-2020 Chair of the 3rd year committee ("VAADAT SHANA") for medical students, Faculty of Health Sciences

2017- Ongoing: Israel Stem Cell Society; organization of annual-meetings and managing of the ISCS

2017- Ongoing: *International Society Experimental Hematology*; taking part in the Publication Committee of ISEH and in the Financial Committee of ISEH

> Participated in the organization of following international meetings, from funding through on-site management:

7th international Stem Cell meeting, Nov. 12-13, 2019, Tel Aviv, Isreal

The 2nd Immuno-oncologinal Meeting of IIS and Cacner, Feb. 22-24, 2022, Haifa, Israel.

Memberships is associations:

2022-ongoing European Hematology Association (EHA)

2015-ongoing International Society Experimental Hematology (ISEH)

2014-ongoing Israel Immunology Society (IIS), Vice-president and treasurer 2021-

2013-ongoing International Society for Stem Cell Research (ISSCR)

2013-ongoing Israel Stem Cell Society (ISCS), Secretary 2020-2022,

2013-2018 Israeli Society for Cancer Research (ISCR) 2013-2014 European Association for Cancer Research (EACR)

Honors

1997 Hebrew University, Dean's list

1999 Hebrew University, B.Sc. with honors

2000 Hebrew University, Polak Prize

2001 Hebrew University, M.Sc. with honors

2003 The Wolf Prize for Excellence in Ph.D. studies

2003- 2006 Selected as an excellent assistant-teacher in the Microbiology Institute

2004-2006 The Clore Scholarship for Doctoral students

2008 Rothschild Fellowship for Post-Doctoral studies

2009-2010 Machiah Fellowship for Post-Doctoral studies

2014- The Ilse Katz Career Development Chair in Health Sciences Research

- **C. Contributions to Science**: I had always enjoyed working with friends, as my complete list of publication show. Hereby I detail some of my personal-works, <u>but truly I consider my collaborative works as major contribution to science.</u>
- 1. Early on PhD studies with Ofer Mandelboim (Hebrew University of Jerusalem), I did several works on Natural-Killer (NK) cells. We did publish several papers regarding NK-cells in human patients and their role in disease. I had generated an NK-reporter mouse by knocking-in a reporter into the NCR1 (NKp46) locus. This NCR1-GFP mouse is the first NK-reporter and NK-specific animal model, it turned pretty useful in the field. My contributions to the NK-filed includes mouse and human in-vivo data.
- 2. uring PostDoc at the laboratory of Derrick Rossi (Harvard Medical School), I got into the field of Hematopoietic Stem Cells (HSCs). We published the extensive molecular-data of transcriptome, directly reprogrammed hematopoietic progenitors into induced-HSCs, and generated an HSC-reporter mouse. The reporter Fgd5-mCherry is portably the first true single-reporter of mouse HSCs, and it turned useful in the field. The direct-reprogramming remains a major interest of the field, with multiple groups taking various pathways. Our molecular-data helped many scientists to better understand HSCs.
- 3. I am part of ImmGen, a consortium of immunologist, since my PostDoc and now as a PI. The ImmGen consortium is a fascinating opportunity for many different immunologists working together and generating molecular and cellular data which are made available for all. ImmGen is highly productive thanks to the combination of multiple laboratories working together not only at late-stages but rather from the very early steps of experimental design.
- 4. My laboratory at the Ben-Gurion University of the Negev generated several contributions, including mapping the Alternative-Splicing landscape in mouse HSCs, Identification of immune-activate HSCs, and the generation of syngeneic Leukemia models. We also have ongoing studies with clinicians at the Soroka medical center.

Recent 5-years publications:

(complete list = https://www.ncbi.nlm.nih.gov/myncbi/1zUeeduK6zpkc/bibliography/public/)

Recent 5-years publications:

- 1. Thapa, R., Elfassy, E., Olender, L., Sharabi, O. & Gazit, R. Rapid activation of hematopoietic stem cells. Stem Cell Res Ther 14, 152 (2023).PMC10245525
- Ofir, N., Mizrakli, Y., Greenshpan, Y., Gepner, Y., Sharabi, O., Tsaban, G., Zelicha, H., Yaskolka Meir, A., Ceglarek, U., Stumvoll, M., Bluher, M., Chassidim, Y., Rudich, A., Reiner-Benaim, A., Shai, I., Shelef, I. & Gazit, R. Vertebrae but not femur marrow fat transiently decreases in response to body weight loss in an 18-month randomized control trial. Bone 171, 116727 (2023)
- 3. Levy, S., Abd Alhadi, M., Azulay, A., Kahana, A., Bujanover, N., Gazit, R., McGargill, M.A., Friedman, L.M. & Hertz, T. FLU-LISA (fluorescence-linked immunosorbent assay): high-throughput antibody profiling using antigen microarrays. Immunol Cell Biol 101, 231-248 (2023)
- 4. Elfassy, E. & Gazit, R. Fresh blood without stem? Blood 141, 2411-2413 (2023)
- Chamo, M., Koren, O., Goldstein, O., Bujanover, N., Keinan, N., Scharff, Y. & Gazit, R. Molecular Mechanisms in Murine Syngeneic Leukemia Stem Cells. Cancers (Basel) 15 (2023).PMC9913241

- Sharabi, O., Greenshpan, Y., Ofir, N., Ottolenghi, A., Levi, T., Olender, L., Adler-Agmon, Z., Porgador, A. & Gazit, R. High throughput screen for the improvement of inducible promoters for tumor microenvironment cues. Sci Rep 12, 7169 (2022).PMC9065017
- 7. Olender, L., Thapa, R. & Gazit, R. Isolation of Murine Myeloid Progenitor Populations by CD34/CD150 Surface Markers. Cells 11 (2022).PMC8834359
- 8. Iraqi, M., Edri, A., Greenshpan, Y., Goldstein, O., Ofir, N., Bolel, P., Abu Ahmad, M., Zektser, M., Campbell, K.S., Rouvio, O., Gazit, R. & Porgador, A. Blocking the PCNA/NKp44 Checkpoint to Stimulate NK Cell Responses to Multiple Myeloma. Int J Mol Sci 23 (2022).PMC9105815
- 9. Greenshpan, Y., Sharabi, O., Yegodayev, K.M., Novoplansky, O., Elkabets, M., Gazit, R. & Porgador, A. The Contribution of the Minimal Promoter Element to the Activity of Synthetic Promoters Mediating CAR Expression in the Tumor Microenvironment. Int J Mol Sci 23 (2022).PMC9266962
- Ottolenghi, A., Bolel, P., Sarkar, R., Greenshpan, Y., Iraqi, M., Ghosh, S., Bhattacharya, B., Taylor, Z.V., Kundu, K., Radinsky, O., Gazit, R., Stepensky, D., Apte, R.N., Voronov, E. & Porgador, A. Life-extended glycosylated IL-2 promotes Treg induction and suppression of autoimmunity. Sci Rep 11, 7676 (2021).PMC8027413
- 11. Olender, L., Levy, K. & Gazit, R. Method for the Generation of Induced Hematopoietic Stem Cells. Methods in molecular biology (Clifton, N.J.) 2185, 399-410 (2021)
- 12. Magidey-Klein, K., Cooper, T.J., Kveler, K., Normand, R., Zhang, T., Timaner, M., Raviv, Z., James, B.P., Gazit, R., Ronai, Z.A., Shen-Orr, S. & Shaked, Y. IL-6 contributes to metastatic switch via the differentiation of monocytic-dendritic progenitors into prometastatic immune cells. J Immunother Cancer 9 (2021).PMC8212411
- 13. Keinan, N., Scharff, Y., Goldstein, O., Chamo, M., Ilic, S. & Gazit, R. Syngeneic leukemia models using lentiviral transgenics. Cell Death Dis 12, 193 (2021).PMC7893004
- Greenshpan, Y., Sharabi, O., Ottolenghi, A., Cahana, A., Kundu, K., K, M.Y., Elkabets, M., Gazit, R. & Porgador, A. Synthetic promoters to induce immune-effectors into the tumor microenvironment. Commun Biol 4, 143 (2021).PMC7846768
- 15. Bujanover, N., Thapa, R., Goldstein, O., Olender, L., Sharabi, O., Milsom, M.D. & Gazit, R. Hypersensitivity response has negligible impact on Hematopoietic Stem Cells. Stem Cell Reports 16, 1884-1893 (2021).PMC8365095
- 16. Tilayov, T., Hingaly, T., Greenshpan, Y., Cohen, S., Akabayov, B., Gazit, R. & Papo, N. Engineering Stem Cell Factor Ligands with Different c-Kit Agonistic Potencies. Molecules 25 (2020).PMC7588011
- 17. Olender, L., Bujanover, N., Sharabi, O., Goldstein, O. & Gazit, R. Cyclosporine H Improves the Multi-Vector Lentiviral Transduction of Murine Haematopoietic Progenitors and Stem Cells. Sci Rep 10, 1812 (2020).PMC7000727
- 18. Iraqi, M., Edri, A., Greenshpan, Y., Kundu, K., Bolel, P., Cahana, A., Ottolenghi, A., Gazit, R., Lobel, L., Braiman, A. & Porgador, A. N-Glycans Mediate the Ebola Virus-GP1 Shielding of Ligands to Immune Receptors and Immune Evasion. Front Cell Infect Microbiol 10, 48 (2020).PMC7068452
- 19. Goldstein, N., Kezerle, Y., Gepner, Y., Haim, Y., Pecht, T., Gazit, R., Polischuk, V., Liberty, I.F., Kirshtein, B., Shaco-Levy, R., Blüher, M. & Rudich, A. Higher Mast Cell Accumulation in Human Adipose Tissues Defines Clinically Favorable Obesity Sub-Phenotypes. Cells 9 (2020).PMC7349306
- 20. Cerqueira, F.M., Kozer, N., Petcherski, A., Baranovski, B.M., Wolf, D., Assali, E.A., Roth, Y., Gazit, R., Barr, H., Lewis, E.C., Las, G. & Shirihai, O.S. MitoTimer-based high-content screen identifies two chemically-related benzothiophene derivatives that enhance basal mitophagy. Biochem J 477, 461-475 (2020)
- 21. ImmGen at 15. Nat Immunol 21, 700-703 (2020)
- 22. Malishev, R., Nandi, S., Smilowicz, D., Bakavayev, S., Engel, S., Bujanover, N., Gazit, R., Metzler-Nolte, N. & Jelinek, R. Interactions between BIM Protein and Beta-Amyloid May Reveal a Crucial Missing Link between Alzheimer's Disease and Neuronal Cell Death. ACS Chem Neurosci (2019)

D. Mentorship and Other Intellectual Contributions

As a PI at the Ben-Gurion University I benefit both research and teaching (listed below).

I do find great interest in mentorship in recent years. Probably following outstanding supervisors for Master, PhD, and PostDoc – I took many things for granted. I did much of a "free-style" mentoring to my students, and managed at the scientific level mostly. I found for my self, in recent years, that I enjoy and benefit much of the personal level too. Thanks to senior and junior fellow of my department, and the scientific community in Israel and international. I appreciate better the values of personal mentoring along our (very) long scientific journey.

I had been appointed as a personal mentor for a fresh (and brilliant) new recruit – Dr. Ofir Cohen. I do learn much with him during last year and a half, and I benefit much the Mentors-class that is an active program at the Ben-Gurion University. I must note that the structured methodology of academic mentoring is not frequently shared at this level of openness, and the individual styles that each PI develops are possibly to improve for many of us. This change over the last years has much of a positive impact both in guiding students, and managing within the academic communities.

My own lab had already gained a dozen Master degrees, 6 PhDs. We are routinely having high-school pupils of the "alpha" program, summer interns, undergrads of Ben-Gurion including life-science, medical lab, and medicine students. Each contribute own way, and we keep an active group with most former lab members.

I am taking an active role in the Israeli Stem Cell Society, a major role at the Israel Immunology Society, and committee member (now for publications, previously finance) of International Society Experimental Hematology. I do find interest and positive impact within our scientific community. I am also pursuing efforts in advancing European Federation immunological Societies (EFiS) educational task-force, realizing the current troubles of public-trust in scientific data. We must do better, as a scientific community, for the local and international public.

Teaching at the Ben-Gurion University:

<u>Undergraduate classes</u>:

- 1. Introduction to Immunology for Life Science, 3rd year Life science (with Alex Braiman and Benyamin Rosental)
- 2. Introduction to Immunology for Medical Students, 2nd year (with Alon Monsenego)
- 3. Nephrology System, for Nursing students, 2nd year (teaching with multiple lecturers)
- 4. Gastrointestinal Immunology, for Nursing students, 2nd year (teaching with multiple lecturers)
- 5. Cancer, from cells to tumors: molecular aspects, for Medical Laboratory 3rd year (teaching with multiple lecturers)
- 6. Introduction to laboratory research, for Medical students 1st year (course of Angel Porgador)
- 7. Immunology, for Pharmacology, 2nd year (with Alex Braiman and Benyamin Rosental) Graduate students (advanced classes):
- 1. Selected problems in the regulation of normal and cancer cells, for Graduate students (with Tomer Cooks)
- 2. Advanced course on Adult Stem Cells
- 3. Flow Cytometry (with Binyamin Rosental)
 - > Taking part in the EFiS teaching task force since 2022.
 - > Enjoy having public-lectures, including kids and elderly, sharing our scientific understanding.

Research Grants {my role in the grant}

2013-2016 CiG; Role of transcription factor Hlf in hematopoietic stem cells 100,000€= 121,000\$ {PI} 2014 ISF; equipment for new faculty 340,000nis= 85,000\$ {PI}

2014-2018 ISF; Reprograming of somatic cells into hematopoietic stem cells: identification of factors and molecular mechanisms 976,000nis= 246,000\$ {PI}

2015 Gif young; HSC Reporter Mouse to Reveal Physiological and patological dynamics of Adult Stem Cells 28,000euro= 31,000\$ {PI}

2016 ISF-INCPM supplement; adding 61,000nis for using INCPM facility {PI}

2016-2019 MOST; Rejuvenate Aged Imune System by Pruning of old Lymphocytess. 1,196,300nis {<u>PI and coordinator for grant to 5 groups</u> (Jacob Dreiher, Angel Porgador, and me from Ben-Gurion University of the Negev, Doron Melamed and Shay Shen-Orr from the Technion)}.

2016-2019 BSF; Hematopoietic Stem Cells within immune development and Activation; 75,000\$ {PI with colaborator Derrick Rossi}.

2017-2019- ICRF; Novel Models for Leukemias in Immune-Competent Mice; 105,000\$ {PI}

2017-2020 DKFZ; Cancerous impact of chronic stress hematopoiesis; 135,000€ {PI with colaborator Michael Milsom}

2020-2023 MOH; Treat Multiple Myeloma sub-clones; 450,000nis {PI with Angel Porgador co-PI}

2021-2026 ISF; Acute and Chronic Stimulation of Hematopoitis Stem Cells; 1,350,000nis {PI}

Institutional Grants

2014 HEZNEK; (seed-grant FOHS) 300,000nis = 75,000\$ {PI with Neta Sal-Man and Uri Greenbaoum (all Co-Pi)}

2015 ISF institutional; FACS, 795,000nis= 200,000\$ {PI with Niv Papo and Amir Aharoni (all Co-PI)} 2018 Wolfson foundation institutional grant; Single Cell Analysis (SCA) Facility at Ben-Gurion University of the Negev for the Study of Nanoscale Phenotypic Variation Across Domains of Life £380,000 {PI with Ramon Birenbaum co-PI, institutional grant}.