
BIOGRAPHICAL SKETCH

NAME: Eran Blacher

POSITION TITLE: Post-doctoral Fellow

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INSTITUTION AND LOCATION	DEGREE	START DATE	END DATE	FIELD OF STUDY
Tel-Aviv University	B.Sc.	10/2007	10/2010	Life-Sciences
Tel-Aviv University	Ph.D.	10/2010	10/2015	Neuroimmunology
Weizmann Institute of Science	Postdoc I	10/2015	01/2019	Brain-microbiome interactions
Stanford University	Postdoc II	01/2019	12/2022	Gut-Brain Axis
Hebrew University of Jerusalem	Assistant Professor	02/2023	Current	Biology of the aging gut

A. Personal Statement

I am a Neuro-immunologist studying how the gut-brain-immune system axis impacts brain pathologies. With an ever-increasing ageing population, neurodegenerative diseases are on the rise and this trend is projected to continue. In all the research carried out, one fundamental question lingers: What causes neurodegeneration? Delving deeper into understanding the environmental factor component of these complex neurological diseases is therefore pertinent.

The human body is a multisystem affected by ageing in numerous ways, some of them are at the interphase of our circulatory system and the environment, such as the gut. Environmental factors like nutrition, lifestyle, sleep and pollutants were shown to critically regulate how we age. My primary scientific goal is to deeply understand the basic cellular processes mediating gut-brain signaling, and to illuminate their connections to phenotypes such as frailty, neurodegeneration and increased susceptibility to various diseases. Specifically, I aim at identifying new peripheral immune interactions and mediators that may serve as novel approaches to treat neurological disorders and to better understand age-related basic biological processes.

B. Positions and Honors

Positions

- 2023-date Assistant professor, Department of Biological Chemistry, The Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem, Edmond J. Safra Campus Givat-Ram, Jerusalem 9190401, Israel.
- 2019-23 Post-doctoral fellow in the laboratory of Prof. Katrin Andreasson, Department of Neurology & Neurological Sciences, Stanford School of Medicine, Stanford University, CA, USA.
- 2015-18 Post-doctoral fellow in the laboratory of Prof. Eran Elinav, Immunology department, Life-Sciences faculty, Weizmann Institute of Science, Rehovot, Israel.
- 2010-15 Ph.D. graduated *Summa cum laude* in the laboratory of Prof. Reuven Stein, Neurobiology department, Life-Sciences faculty, under the Dean's list honors direct Ph.D. program for outstanding students of Tel-Aviv University. **Received full Ph.D. fellowship from the Argentina foundation.**
- 2007-10 B.Sc. graduated *Magna cum laude* in the research program for excelling students, Life Sciences Faculty, Tel Aviv University. The program requires conducting research projects and emphasizes research procedures, data analysis, and critical reading of scientific publications. Graduated with honors. Was awarded a yearly scholarship for excellence.
- 2007-10 Guide and educational programs writer at "Havayeda-TEVA", a science museum in Holon, Israel, which included teaching and illustrating scientific themes for dozens of groups from different backgrounds.
- 2007-08 Teacher for teenagers with difficulties, "Ometz" program, "Rabin" Highschool, Azor, Israel.
- 2004-07 Military service: Journalist and foreign news editor at the Israeli Air-Force Magazine (Sergeant).

Other Experience and Professional Memberships

- 2021-date American Association for the Advancement of Science (AAAS). Member # 20368158.
2019 Stanford University Scientific Teaching Institute, the Science Education Partnership and Assessment Laboratory (SEPAL) of San Francisco State University.
2019-20 Professional member, American Heart Association AHA/ASA.
2018-date Associate Faculty Member for Physiology, Faculty Opinions (“F1000”).
2014- date Israeli Society for Neuroscience (ISFN).

Honors

- 2021 Awarded the **Grand Prize** in the inaugural **NOSTER & Science** Microbiome competition. Grand Prize winner is awarded a cash prize in the amount of \$25,000 and travel and accommodation for the prize ceremony. The Grand Prize winner also receives a free five years digital subscription to *Science*, and have their winning essay published in *Science*.
- 2020-23 **Marie Sklodowska-Curie European Global Fellowship**. Horizon 2020, H2020-MSCA-IF-2019, Proposal 888494, ‘immunogut’. Title: *Unraveling the role of aging in post-stroke gut-brain axis signaling*.
- 2019-20 Stanford School of Medicine Dean's Postdoctoral Fellowship, Stanford, CA, USA.
2017-19 Dean of Faculty Fellowship. Weizmann Institute of Science, Israel.
2016 Research Fellowship from TEVA, The National Network of Excellence in Neuroscience (NNE) 10/01/2015-10/01/2016 Targeting CD38 for Neurodegenerative diseases treatment – denied.
2015 The Life Science Faculty Award for Excellence Achievements in Research. Tel-Aviv University, Israel.
2015 Iafa Keydar Cancer Research Prize, Tel-Aviv University, Israel.
2015 TAU Cancer Biology Research Center (CBRC) Scholarship, Israel.
2015 Sagol School of Neuroscience Scholarship, Tel-Aviv University, Israel.
2015 Ela Kodesh Cancer Research Institute Scholarship, Israel.
2013 Anat Krauskopf travel fund award, Israel.
2013 Adams Super-Center for Brain Studies Scholarship, Israel.
2013 Ela Kodesh Cancer Research Institute Scholarship, Israel.
2012 TAU Cancer Biology Research Center (CBRC) Scholarship, Israel.
2011-15 The Dean’s list honors direct Ph.D. program for outstanding students of Tel-Aviv University. Received full Ph.D. fellowship from the Argentina foundation.
2012 Cold Spring Harbor Laboratory Travel Scholarship, CSHL, NY, USA
2010 Joan and Jaime Constantiner Institute for Molecular Genetics Scholarship, Israel.
2010 Dean award for excellence, Tel-Aviv University, Israel.

C. Contribution to Science

The Microbiome-gut-brain axis

My first postdoctoral work was carried out with Prof. Eran Elinav at the Weizmann Institute of Science, Immunology Department. I found the first proofs of the microbiome involvement in Amyotrophic Lateral Sclerosis (ALS) pathogenesis and identified its mechanism by defined commensal strains and their biochemical activity. I utilized these findings for the first successful microbiome treatment in murine ALS, consisting of defined live bacterial therapy and metabolite supplementation. I also demonstrated similar findings in human ALS patients, including skewed metabolite levels in their nervous system that can serve as a basis for new human postbiotic therapy. This study was published in *Nature*. Moreover, I studied the effect of hyperglycemia on gut barrier dysfunction and wrote 4 review articles on the host-microbiome interactions in health and disease.

1. **Blacher E**, Tsai C, Litichevskiy L, Shipony Z, Agbaegbu Iwuka C, Markus Schneider K, Chuluun B, Heller CH, Menon V, Thaïss CA and Andreasson KI. (2021) Aging disrupts homeostatic circadian gene regulation and function in macrophages. *Nature Immunology* 23 (2): 229-236. **Featured in Nature immunology News & Views, Curtis and Carroll, Aging alters rhythms in immunity. doi.org/10.1038/s41590-021-01099-6 and in McRae HM, Hargreaves DC. Old macrophages lose their (circadian) rhythm. Trends Immunol. 2022 Apr;43(4):265-267. doi: 10.1016/j.it.2022.02.005. Epub 2022 Mar 10.**

2. **Blacher E.** (2021) Can microbes combat neurodegeneration? Identifying a missing link between microbiome and metabolites in ALS. *Science* 373 (6551): 172-173. **NOSTER & Science Microbiome Grand Prize Essay.**
3. **Blacher E***, Bashiardes S*, Rothschild D*, Shapiro H*, Mor U, Dori-Bachash M, Kleimeyer C, Moresi C, Harnik Y, Zur M, Zabari M, Ben-Zeev Brik R, Kviatcovsky D, Zmora N, Cohen Y, Bar N, Levi I, Amar N, Mehlman T, Brandis A, Biton I, Kuperman Y, Tsoory M, Alfahel L, Harmelin A, Schwartz M, Israelson A, Arike L, Johansson M. E. V, Hansson G. C, Gotkine M, Segal E and Elinav E. (2019) Potential roles of gut microbiome and metabolites in modulating ALS in mice. *Nature* 572: 474-480. **Featured in Bucci, M. A NAmE-tag for ALS. Nat Chem Biol 15, 933 (2019). <https://doi.org/10.1038/s41589-019-0374-7> and in more than a hundred of general media publications and commentaries, including the BBC news, The Guardian and more.**
4. Thaiss CA, Levy M, Grosheva I, Zheng D, Soffer E, **Blacher E**, Braverman S, Tengeler AC, Barak O, Elazar M, Ben-Zeev R, Lehavi-Regev D, Katz MN, Pevsner-Fischer M, Gertler A, Halpern Z, Harmelin A, Amar S, Serradas P, Grosfeld A, Shapiro H, Geiger B and Elinav E. (2018). Hyperglycemia drives intestinal barrier dysfunction and risk for enteric infection. *Science* 359: 1376-1383.
5. Kundu P*, **Blacher E***, Petresson S and Elinav E. (2017) Our gut microbiome: the evolving inner self. *Cell* 171: 1481-1493.
6. **Blacher E***, Levy M*, Tatirovsky E and Elinav E. (2017). Microbiome-modulated metabolites at the interface of host immunity. *Journal of Immunology*. 98: 572-580.
7. Pevsner-Fischer M*, **Blacher E***, Tatirovsky E, Ben-Dov IZ and Elinav E (2016) The gut microbiome and hypertension. *Current Opinion in Nephrology and Hypertension*. 25: 1062-4821.
8. Levy M*, **Blacher E***, Tatirovsky E and Elinav E. (2017). Microbiome, metabolites and host immunity. *Current Opinion in Microbiology*. 35: 8-15.

The role of CD38 and NAD⁺ metabolism in cancer and brain pathologies

During my Ph.D. I have initiated and established experimental systems, designed, conducted and analyzed experimental approaches aimed at establishing CD38 targeting as a novel therapeutic strategy for brain pathologies, including cancer and Alzheimer's disease. I showed that genetic loss of CD38 attenuated glioma progression and enhanced the lifespan of glioma-bearing mice. Additionally, I identified a novel small molecule CD38 inhibitor that effectively phenocopied my previous findings in vivo and attenuated glioma and metastatic melanoma progression. Since up today there is no effective treatment against glioma, my findings are very important as they suggest that CD38 targeting may be used as therapeutic approach. During my Ph.D. I have published 10 research papers in peer-reviewed journals, 4 of which as a first co-author.

9. Ben Baruch B, Mantsur E, Franco-Barraza J, **Blacher E**, Cukierman E and Stein R. (2020) CD38 in cancer-associated fibroblasts promotes pro-tumoral activity. *Laboratory Investigation*. 100: 1517-1531.
10. Ben Baruch B*, **Blacher E***, Shwartz H, Vaknine H, Erez N and Stein R. (2018). Stromal CD38 regulates progression of primary melanoma and generation of spontaneous metastasis. *Oncotarget*. 9: 31797-31811.
11. **Blacher E**, Dadali T, Haupenthal V. J, Grimm M. O. W, Hartmann T, Lund F. E., Stein R and Levy A. (2015). Alzheimer's disease pathology is attenuated in a CD38-deficient mouse model. *Annals of Neurology*. 78: 88-103.
12. **Blacher E**, Ben Baruch B, Levy A, Geva N, Green K. D, Garneau-Tsodikova S, Fridman M. and Stein R. (2015). Inhibition of glioma progression by a newly discovered CD38 inhibitor. *International Journal of Cancer*. 136: 1422-1433.
13. **Blacher E**, Levy A, Ben Baruch B, Green K. D, Garneau-Tsodikova S, Fridman M. and Stein R. (2015). Targeting CD38 in the tumor microenvironment; a novel approach to treat glioma. *Cancer Cell and Microenvironment*. 2: 1-6.

14. Levy A, **Blacher E**, Vaknine H, Lund F. E, Stein R and Mayo L. (2012). CD38 deficiency in the tumor microenvironment attenuates glioma progression and modulates features of tumor-associated microglia/macrophages. *Neuro-Oncology*. 14: 1037-1049.

Studying the basic biology of cancer, metastases formation and programmed cell death

During my undergraduate and first graduate years I studied basic cell biology questions that can be translated to potential cancer therapies. I sought to understand the interplay between resident brain cells such as astrocytes and cancer cells that can be located in remote areas of the body, yet metastasize to the brain. I was involved in studies testing chemical derivation of known chemotherapy drugs to improve its efficacy and bioavailability and reduce potential side-effects in collaboration with Prof. Micha Fridman from the School of Chemistry at Tel-Aviv University. As understanding the molecular basis of programmed cell death is one of the fundamental processes in developing novel strategies to treat cancer, I studied also the redistribution of nuclear proteins after stress induced by chemotherapy agents, and discovered a novel function for the pro-apoptotic proteins Bak and Bax in regulating this controlled release of nuclear proteins prior cell-death.

15. Lautman Z*, Winetraub Y*, **Blacher E***, Terem I, Yu C, Chibukhchyan A, Marshel JH and de la Zerda A. (2022). Intravital 3D visualization and segmentation of murine neural networks at micron resolution *Scientific Reports* 12, 13130.
16. Schwartz H, **Blacher E**, Amer M, Livneh N, Abramovitz L, Klein A, Ben-Shushan D, Sofer S, Blazquez R, Barrantes-Freer A, Muller M, Muller-Decker K, Stein R, Tsarfaty G, Satchi-Fainaro R, Umansky V, Pukrop T and Erez N. (2016) Incipient melanoma brain metastases instigate astrogliosis and neuroinflammation. *Cancer Research*. 15: 4359-4371.
17. Shaul P, Steinbuch K, **Blacher E**, Stein R and Fridman M. (2015). Exploring the effects of glycosylation and etherification of the side-chains of the anti-cancer drug mitoxantrone. *ChemMedChem*. 10: 1528-1538.
18. Aizman E, **Blacher E**, Ben-Moshe O, Kogan T, Kloog Y and Mor A. (2013). Therapeutic effect of farnesylthiosalicylic acid on adjuvant-induced arthritis in rats through suppressed release of inflammatory cytokines. *Clinical and Experimental Immunology* .175: 458-467.
19. Lindenboim L, **Blacher E**, Borner C and Stein R. (2010). Regulation of stress-induced nuclear proteins' redistribution: a new function of Bax and Bak uncoupled from Bcl-x_L. *Cell Death and Differentiation*. 17: 346–359.

Work in progress

20. **Blacher E**, Agbaegbu Iweka C, Wang Q and Andreasson KI. (2022) Aging increases post-stroke inflammation in the gut through sustained norepinephrine signaling and TREM1 activation (In preparations).
21. **Blacher E**, Agbaegbu Iweka C, Tsai C, Wang Q and Andreasson KI. (2022) Dual fronts of inflammation after stroke offer new therapeutic opportunities. *Nature Reviews Immunology* (In preparations - advanced).
22. Agbaegbu Iweka C, **Blacher E** and Andreasson KI. (2022) Reduced expression of the cell intrinsic clock protein, Bmal1, in myeloid cells accelerates cognitive decline and alters microglial function in aging mice (In preparations).
23. **Blacher E** (2022) Harnessing the microbiome to treat age-associated diseases. (2022) *Microorganisms* (In preparations).
24. Wilson EN, Swarovski MS, McReynolds MR, Wang Q, Zera KA, Chaney A, Gauba E, Minhas PS, **Blacher E**, Iweka CA, Panchal M, Cropper H, Jain P, Liu Q, Mehta SS, Zuckerman AJ, Xin M, Umans J, Huang J, Benitez JAR, Durairaj AS, Serrano GE, Beach TG, James ML, Buckwalter MS, Rabinowitz JD and Andreasson IA (2021), TREM1 disrupts myeloid bioenergetics in models of aging and Alzheimer's disease. *Science* (submitted).

List of publications in PubMed:

<https://www.ncbi.nlm.nih.gov/myncbi/1xcerXfPwr9kt/bibliography/public/>

D. Independent grants & Research funds

2023-2026 The Azrieli Foundation Faculty Fellowship (\$213K total)

E. Additional Information: Scholastic Performance

Critical review of scientific research manuscripts for international journals

- 2022 **mSystems**, mSystems01223-21.
2021 **Nutrients**, Nutrients-1103371. **Journal of Gerontology: Biological Sciences**, JGBS-2021-250.
2020 **Microorganisms**, microorganisms-815464.
2019 **Medical Sciences**, medsci-644000, **Nutrients**, Nutrients-624920, Nutrients-596607, **Nature**, 2018-08-11716.
2018 **Nature Medicine**, NMED-L85740, **The Lancet**, THELANCET-D-18-00382.
2017 **Cell**, CELL-D-16-01068R1, **Science Translational Medicine**, aan5662.
2016 **Nature**, 2016-07-09627.

Participation in colloquia

- 2022 “Follow your gut: Microbiome-gut-brain interactions in disease” *Proteintech’s ECR virtual mini symposium* – **Keynote speaker**. The immune system-gut-brain axis: environmental impacts on aging and neurological disorders – *Johns Hopkins University School of Medicine Microbiome Forum* - **Invited speaker**.
- 2021 Can microbes combat neurodegeneration? – *Science* magazine webinar and Noster & *Science* Microbiome prize ceremony - **Invited speaker**. The intestine as a second front of innate immune activation after stroke. Joint Leadership Group AHA/Allen Initiative in Brain Health & Cognitive Impairment and Stanford Cardiovascular Institute (CVI) Early Career Research Roundtable - **Invited speaker**. Aging disrupts homeostatic circadian gene regulation and function in macrophages. Joint Leadership Group AHA/Allen Initiative in Brain Health & Cognitive Impairment - **Invited speaker**. See and be Seen – The 2nd Non-Job-Talk meeting in Biology by the Israel Young Academy - **panelist speaker**.
- 2020 The role of the gut microbiome and associated metabolites in Amyotrophic Lateral Sclerosis (ALS). *ScienceAbroad Life Sciences Symposium* - **Panelist speaker**. The 28th Tel-Aviv University Alzheimer’s disease conference - **Invited speaker**.
Neurobiology department, Tel-Aviv University, Israel. **Neurobiology guest speaker**. The Faculty of Medicine, The Hebrew University of Jerusalem, Israel. **Clinical Neurobiology guest speaker**.
- 2019 Episode 287: Microbes, rocks, and lost cities, Stanford’s science podcast “Goggles optional” – **Invited speaker**. Aging disrupts homeostatic circadian gene regulation in macrophages, Bay Area Aging Meeting (BAAM), Stanford University, Stanford, CA, USA – **Abstract**. ROSMAP, Rush Alzheimer’s Disease Center, Rush University, Chicago, IL, USA. **Abstract**.
- 2018 Personalized nutrition by prediction of glycemic responses, Tel-Aviv, Israel. Lecture to family doctors of the “Clalit” HMO – **Invited speaker**.
- 2017 Host-microbiome interactions in health and disease, Jena, Germany, The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) annual retreat – **Invited keynote speaker**.
- 2015 Inhibition of glioma progression by a newly discovered CD38 inhibitor, Bilbao, Spain, XII European meeting on Glial Cells in Health and Disease – **Abstract**.
- 2014 CD38 as a potential target for Alzheimer disease, Tel-Aviv University, Israel, the 22nd Tel-Aviv University Alzheimer’s disease conference – **Speaker**.
- 2013 CD38 deficiency ameliorates Alzheimer’s disease-related pathology in mouse model for Alzheimer’s disease, Sarteano-Siena, Italy; The 8th Tuscany conference on Genetic profiling, resistance mechanism, and novel treatment concepts in cancer – **Speaker**. Berlin, Germany, XI European meeting on Glial Cells in Health and Disease –

Abstract. CD38 Deficiency attenuates melanoma progression, Safed, Israel, 2013 biennial retreat for the Cancer Biology Research Center – **Selected student talk.**

- 2012 Role of CD38 in glioma progression, Banbury conference center, Lloyd Harbor, NY, Cold Spring Harbor Laboratory advanced course in Brain Tumors – **Speaker.** CD38 Deficiency attenuates Alzheimer's disease pathology in a mouse model, Tel-Aviv University, Israel, Brain Plasticity Symposium, Sagol School of Neuroscience – **Abstract.**
- 2011 Characterization of new CD38 inhibitors, Sarteano-Siena, Italy, the 7th Tuscany conference on Genetic profiling, resistance mechanism, and novel treatment concepts in cancer – **Speaker.** Targeting CD38 as a novel approach to attenuate microglia-associated brain pathologies, Eilat, Israel, the 6th Congress of the Federation of the Israel Societies for Experimental Biology - FISEB (ILANIT) – **Abstract.**