BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Shahar Lev-Ari, PhD

eRA COMMONS USERNAME (credential, e.g., agency login):

POSITION TITLE: Member, Department of Health Promotion, Sackler Faculty of Medicine, Tel Aviv University, Israel. Visiting Scholar, Department of Genetics, Stanford University, US

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
Hebrew University, Jerusalem, Israel	LLB	9/1995	Law
Tel Aviv University, Tel Aviv, Israel	MSc	2/2004	Pharmacology&Physiolog y
Tel Aviv University, Tel Aviv, Israel	PhD	2/2008	General Medicine

A. Personal Statement

I am a member and former Chair of the Department of Health Promotion, in the School of Public Health, in the Faculty of Medicine at Tel-Aviv University, former director, and founder of the Integrative Medicine Center & Research Laboratory at the Tel-Aviv Medical Center, and Head of the Health Promotion Unit in the Integrated Cancer Prevention Center. My training is in cellular biology, integrative medicine, intervention research, and health promotion science. The goal of my research is to unravel the biology, physiology, and psychology of integrative medicine approaches and translate findings into interventions that effectively target salutogenic mechanisms underpinning the biopsychology of well-being. In this regard, I have developed the mechanistic foundation of integrative medicine approaches in hospital settings as an integral part of the Institute of Oncology at the Tel-Aviv Medical Center. I have developed methodological expertise in the design and implementation of clinical trials of integrative mind-body interventions for reducing stress, enhancing well-being, and empowering health promotion behaviors, as well as in advanced statistical analyses of clinical outcomes, individual risk factors, and inflammatory pathways and moderators. I have so far mentored more than 50 graduate and postgraduate students and won the Dean's Award for Teaching Excellence. To complement my expertise in clinical research, I trained in integrative medicine approaches, including Chinese medicine and shiatsu, meditation, and whole-person lifestyle and have conducted over 15 years of health promotion consultancy and mindfulness-based programs for patients in both hospital and community-based integrative medicine settings. I have successfully led interdisciplinary research teams, including experimental studies and spearheaded biostatistical analyses leading to the publication of more than 70 peer-reviewed scientific manuscripts and book chapters in high-impact journals, including the Journal of Clinical Oncology, Clinical Cancer Research and Jama Network Open. I received the Outstanding Israeli Researcher Award for Complementary and Integrative Medicine, was appointed to edit the handbook of the Israel Cancer Society for Integrative Medicine and invited to serve as an editorial board member of the European Journal of Integrative Medicine and a section editor for the Journal of Clinical Medicine.

We have recently obtained a one-of-a-kind opportunity to assess the long-term effects of Tony Robbins' "Date With Destiny" (DWD), one of the largest virtual mind-body interventions worldwide, on stress and wellbeing over the course of one year and to develop predictive models of participants' stress and well-being. Using a precision-health approach with known biomarkers (biological, psychosocial, and physiological), we will predict long-term changes in stress and well-being following mind-body interventions and develop personalized mindbody techniques. I will co-lead this project with Prof. Michael Snyder's Lab, a global leader in precision health at Stanford University. "I have been collaborating with Prof. Snyder and his team on precision health mind-body research since 2019. During my sabbatical in 2022, I initiated and co-lead the 'LastingChange' as a visiting scholar at Dr. Snyder's lab.

Ongoing/Recent funded projects include:

Chief scientist, Ministry of Education 0601445891, Lev-Ari(PI), 1.1.22 – 6.30.23 Development of functional resilience index of schools in Israel.

Israel Cancer Association 20211200, Lev-Ari (PI), 1.1.20-12.31.21 The effect of IBSR on well-being of BRCA1/2 carriers, during COVID-19 pandemic.

Citations:

- Landau C, Novak AM, Ganz AB, Rolnik B, Friedman E, Lev-Ari S. Effect of Inquiry-Based Stress Reduction on Well-being and Views on Risk-Reducing Surgery Among Women With BRCA Variants in Israel: A Randomized Clinical Trial. JAMA Netw Open. 2021;4(12):e2139670. doi:10.1001/jamanetworkopen.2021.39670
- 2. Lev-ari, S.; Gepner, Y.; Goldbourt, U. Dissatisfaction with Married Life in Men Is Related to Increased Stroke and All-Cause Mortality. J. Clin. Med. 2021, 10, 1729. https://doi.org/10.3390/jcm10081729
- 3. Zadok-Gurman T, Jakobovich R, Dvash E, Zafrani K, Rolnik B, Ganz AB, **Lev-Ari S**. Effect of Inquiry-Based Stress Reduction (IBSR) Intervention on Well-Being, Resilience and Burnout of Teachers during the COVID-19 Pandemic. Int J Environ Res Public Health. 2021 Apr 1;18(7):3689.
- Bernstein E*, Lev-Ari S*, Shapira S, Leshno A, Sommer U, Al-Shamsi H, Shaked M, Segal O, Galazan L, Hay-Levy M, Sror M, Harlap-Gat A, Peer M, Moshkowitz M, Wolf I, Liberman E, Shenberg G, Gur E, Elran H, Melinger G, Mashiah J, Isakov O, Zrifin E, Gluck N, Dekel R, Kleinman S, Aviram G, Blachar A, Kessler A, Golan O, Geva R, Yossepowitch O, Neugut AI, Arber N. Data From a One-Stop-Shop Comprehensive Cancer Screening Center. J Clin Oncol. 2023 May 10;41(14):2503-2510. doi: 10.1200/JCO.22.00938.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2022-Present Visiting Scholar, Department of Genetics, Stanford University School of Medicine Head, Health Promotion Unit, Integrated Cancer Prevention Center (ICPC), Tel-Aviv 2020-Present Medical Center, Israel Chair of Department of Health Promotion. Faculty of Medicine. Tel Aviv University. Israel 2017-2021 2014-Present Asst. Professor, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Israel 2011-2019 Director, Center of Complementary and Integrative Medicine, Institute of Oncology, Tel Aviv Medical Center Head, laboratory of medicinal herbs and cancer research, Institute of Oncology, Tel Aviv 2010-2019 Medical Center Lecturer, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Israel 2009-2014 2008-2010 Research Manager, Complementary Medicine Unit, Tel Aviv Medical Center

Selected Recent Advisory Committees

- 2012-Present Editorial Board member, European Journal of Integrative Medicine
- 2015-Present Advisory Board Member, Israeli Cancer Society
- 2018-Present Editorial Member, Israeli Journal of Health Education and Promotion
- 2018-Present Board Member, Israeli Health Education and Promotion Society
- 2020-Present Academic Committee Board Member, Israeli Healthy Cities Initiative
- 2021-Present Section Editor, Journal of Clinical Medicine
- 2021-Present Special Issue Editor, *Biology*

Professional Memberships

- 2008-Present Israeli Society for Cancer Research
- 2009-Present Israel Cancer Society
- 2009-Present American Association for Cancer Research
- 2018-Present Israeli Health Education and Promotion Society
- 2020-Present Society for Theory and Research on Salutogenesis

2021-Present International Union for Health Promotion and Education (IUHPE)

2021-Present Multi-national Resilience and Well-being Center

<u>Honors</u>

- 2005 NIH-NCCAM Travel Award
- 2005 Joint American-Israeli Conference, awarded 3rd prize
- 2006 American Society of Integrative Oncology (SIO), Travel Award
- 2010 Outstanding Israeli Researcher Award, Israeli Society for Complementary and Integrative Medicine, under the auspices of the Israeli Medical Association.
- 2016 Honorarium Lecturer Award, Jangheung International Integrative Medicine Conference
- 2017 Dean's Award for Teaching Excellence, Faculty of medicine, Tel-Aviv University.
- 2021 Member, Global Working Group of Mental Health Promotion.

B. Contributions to Science

1. Development of integrative approaches and mind-body interventions research. A primary focus of my research has been to unravel the mechanism of integrative medicine approaches and translate findings into interventions that effectively target salutogenic mechanisms underpinning the biopsychology of well-being. In much of my research I have concentrated on mind-body approaches and developed the research protocol of Inquiry-Based Stress Reduction (IBSR) technique, based on the skills and principles of self-inquiry, mindfulness, cognitive reframing, and behavioral change. Our study was the first RCT to demonstrate the impact of a non-pharmacological intervention on the views regarding risk-reducing (and potentially lifesaving) surgeries among people with BRCA variants. We have shown that in the general population, practicing the IBSR technique was associated with improved psychopathologic symptoms, improved happiness, and perceived quality of life. Additionally, it reduced occupational burnout in teachers and improved the subjective and psychology and uselbeing of teachers during the COVID-19 pandemic. We ensured the highest standards of study methodology in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement for randomized clinical trials and the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) guidelines.

- Landau C, Novak AM, Ganz AB, Rolnik B, Friedman E, Lev-Ari S. Effect of Inquiry-Based Stress Reduction on Well-being and Views on Risk-Reducing Surgery Among Women With BRCA Variants in Israel: A Randomized Clinical Trial. JAMA Netw Open. 2021;4(12):e2139670. doi:10.1001/jamanetworkopen.2021.39670
- Zadok-Gurman T, Jakobovich R, Dvash E, Zafrani K, Rolnik B, Ganz AB, Lev-Ari S. Effect of Inquiry-Based Stress Reduction (IBSR) Intervention on Well-Being, Resilience and Burnout of Teachers during the COVID-19 Pandemic. Int J Environ Res Public Health. 2021 Apr 1;18(7):3689.
- 3. Ricon-Becker I, Fogel E, Cole SW, Haldar R, **Lev-Ari S**, Gidron Y. Tone it down: vagal nerve parasympathetic activity is associated with pro-inflammatory and anti-viral factors in breast cancer patients. Comprehensive Psychoneuroendocrinology (2021 Elsevier Ltd.), 2021,
- Feldman O, Goldstien E, Rolnik B, Ganz AB, Lev-Ari S. Inquiry Based Stress Reduction (IBSR) Improves Overall Stuttering Experience among Adults Who Stutter: A Randomized Controlled Trial. J Clin Med. 2021 May 18;10(10):2187. doi: 10.3390/jcm10102187

2. Investigating the mediators and outcomes of resilience and well-being in a community setting is a secondary focus of my research. Supported by a grant from the *Chief Scientist of the Israeli Ministry of Education*, Prof. Adini and I developed a functional resilience index for schools in Israel. Our research examined the psychosocial aspects and communication challenges faced by key stakeholders in the Israeli education system during the COVID-19 pandemic. Our findings emphasize the need for tailored capacity-building and resilience intervention programs to enhance well-being and reduce distress among stakeholders, particularly those who are most vulnerable. In an additional study conducted during the pandemic, we explored the relationship between resilience and participation in online sports programs, highlighting the importance of maintaining such programs to support adolescents' resilience. Additionally, we collaborated with school systems to study the effects of Cognitive Behavioral Group Therapy (CBT) on children's self-esteem. This study highlights the potential benefits of CBT in enhancing self-esteem among children and indicates the feasibility of delivering the CBT protocol in a school setting. Overall, these studies have made significant contributions to understanding various psychosocial aspects and interventions in response to the COVID-19

pandemic, encompassing education, sports programs, therapy, and web-based activities across different age groups, and their implications on resilience and well-being in community setting.

- Kaim A, Lev-Ari S*, Adini B*. Distress following the COVID-19 Pandemic among Schools' Stakeholders: Psychosocial Aspects and Communication. International Journal of Environmental Research and Public Health. 2023; 20(6):4837. https://doi.org/10.3390/ijerph20064837
- Constantini, K.; Markus, I.; Epel, N.; Jakobovich, R.; Gepner, Y.; Lev-Ari, S. Continued Participation of Israeli Adolescents in Online Sports Programs during the COVID-19 Pandemic Is Associated with Higher Resilience. Int. J. Environ. Res. Public Health 2021, 18, 4386. https://doi.org/10.3390/ijerph18084386.
- 3. Epel N, Zohar AA, Artom A, Novak AM, Lev-Ari S. The Effect of Cognitive Behavioral Group Therapy on Children's Self-Esteem. Children (Basel). 2021 Oct 24;8(11):958. doi: 10.3390/children8110958.
- Novak AM, Katz D, Bitan M, Lev-ari S. The association between sense of coherence and adherence of individuals to social distancing guidelines in the time of COVID-19. International Journal of Environmental Research and Public Health 2022 Jun 30;19(13):8041

3. Investigation of health behaviors and psychosocial factors in healthy aging and longevity. In view of my expertise in health promotion and population studies, as well as in the application of advanced statistical techniques, I have made significant scientific contributions. These contributions have revealed the pivotal role of marital satisfaction in mortality risk, as demonstrated by large-scale investigations involving over 10,000 participants spanning four decades. The findings highlight that individuals dissatisfied with their marriages face an increased long-term risk of stroke and all-cause mortality, emphasizing the importance of nurturing healthy relationships and advocating for interventions targeting marital satisfaction in health promotion strategies. Furthermore, our research with Prof. Goldbourt on midlife predictors of longevity has deepened our understanding of the intricate interplay between psychosocial and physiological factors in health outcomes. This knowledge has informed evidence-based approaches to improving population health. Our study on exceptional patients has shed light on the recurring theme of active patient empowerment and engagement in survivorship, supporting the adoption of personalized, patient-centered approaches. Moreover, the study on web-based activities for older adults during the COVID-19 pandemic has underscored the significance of providing engaging and accessible alternatives to in-person activities. Collectively, these contributions have advanced scientific knowledge and influenced the development of strategies aimed at promoting longevity and improving overall health outcomes.

- 1. Lev-ari, S.; Gepner, Y.; Goldbourt, U. Dissatisfaction with Married Life in Men Is Related to Increased Stroke and All-Cause Mortality. J. Clin. Med. 2021, 10, 1729. https://doi.org/10.3390/jcm10081729
- Lev-Ari S, Novak AM, Zemer A, Gerber Y, Goldbourt U. Reaching 80 Years of Age: Clinical, Behavioral, and Psychosocial Related Risk Factors in a Large Cohort of Israeli Working Men. J Clin Med. 2021 Dec 5;10(23):5706. doi: 10.3390/jcm10235706.
- Frenkel M, Lev-Ari S, Engebretson J, Peterson N, Maimon Y, Cohen L, Kacen L. Activism among exceptional patients with cancer. Supportive care in cancer 2010 19(8):1125-1132. IF 3.359; Rehabilitation in SCIE edition ; Rank 17/68; Q1; Times Cited: 23
- Cohen-Mansfield J, Muff A, Meschiany G, Lev-Ari S. Adequacy of Web-Based Activities as a Substitute for In-Person Activities for Older Persons During the COVID-19 Pandemic: Survey Study. Journal of medical internet research 2021 Feb 16;23(2): e27687.

4. Enhancing Cancer Prevention: Integrating Early Detection, Biomarkers, and Patient-Centered Approaches. In a recent study published in the *Journal of Clinical Oncology*, we conducted proof-of-concept research that introduced a comprehensive one-stop-shop approach to cancer screening. The results demonstrated the successful detection of early-stage cancers, which holds the potential for significant reductions in morbidity, mortality, and healthcare costs. Furthermore, our screening program incorporated the evaluation of various health behaviors, including diet, physical activity, smoking status, and alcohol intake, providing comprehensive support for both primary and secondary prevention strategies. Notably, we introduced a CD24/CD11b-based blood test as a potential screening tool for hematological malignancies, with significantly higher levels observed in cancer patients compared to healthy individuals. In addition, elevated levels of CRP were found to be associated with higher CD24/CD11b expression among healthy participants. These findings contribute to the development and optimization of the CD24/CD11b biomarker as a potential screening test for early cancer detection in the healthy population, providing insights for further research in this

area. In addition, our large-scale longitudinal population study revealed evidence of the association between excess body weight and an increased risk of colon cancer, as well as a decreased risk of lung cancer. These findings contribute valuable evidence to the field and shed light on the complex relationship between body weight and specific cancer types. This transformative approach prioritizes prevention, early detection, and patient empowerment, ultimately leading to improved outcomes and a better quality of life for individuals affected by cancer.

- Bernstein E*, Lev-Ari S*, Shapira S, Leshno A, Sommer U, Al-Shamsi H, Shaked M, Segal O, Galazan L, Hay-Levy M, Sror M, Harlap-Gat A, Peer M, Moshkowitz M, Wolf I, Liberman E, Shenberg G, Gur E, Elran H, Melinger G, Mashiah J, Isakov O, Zrifin E, Gluck N, Dekel R, Kleinman S, Aviram G, Blachar A, Kessler A, Golan O, Geva R, Yossepowitch O, Neugut AI, Arber N. Data From a One-Stop-Shop Comprehensive Cancer Screening Center. J Clin Oncol. 2023 May 10;41(14):2503-2510. doi: 10.1200/JCO.22.00938.
- Gepner Y, Lev-ari S, Goldbourt U. Excess Body Weight and Long-Term Incidence of Lung and Colon Cancer in Men; Follow-Up Study of 43 Years. International Journal of Environmental Research and Public Health. 2021; 18(19):10418. https://doi.org/10.3390/ijerph181910418
- 3. Shapiara S, Aiger G, Ohayon A, Kazanov D, Mdah F, Ben-Simon M, Hay-Levy M, Banon L, Laskov I, Mashiah J, Lev Ari S*, Arber N* Predictors of the CD24/CD11b Biomarker among Healthy Subjects Journal of personalized medicine. 2021, 11, 939. PMID: 34575716
- Shapiara S, Yaakobi H, Herishanu Y, Peri H, Avivi I, Itchaki G, Hay-Levy M, Raanani P, Aiger G, Mashiah J, Lev Ari S*, Arber N* Feasibly of CD24/CD11b as a screening test for hematological malignancies

5. Investigating the role of phyto-bioactive compounds in regulating inflammatory pathways and modulating key chemo-radio resistance. Medicinal herbs and their derivative phyto-bioactive compounds are increasingly recognized as potential treatments for cancer. As the head of the Laboratory of Herbal Medicine and Cancer Research, I led an Israeli delegation to India, which signed a collaboration memorandum between the Central Council for Research in Ayurvedic Sciences (CCRAS), the Ministry of Ayush, the Government of India, and the Tel-Aviv Medical Center. Supported by grants from the *Israel Cancer Organization* and the renowned *Edmond de Rothschild Foundation*, we conducted multiple innovative studies to assess the role of traditional medicinal herbs, such as Curcuma Longa, Moringa Oleifera, and Boswellia Serrata, in inflammatory and cancer prevention pathways. Our findings demonstrated that the combination of medicinal herbs with chemotherapy and radiotherapy synergistically inhibited the survival, migration, and invasion properties of various cancer cells. Additionally, we revealed the mode of action of phyto-bioactive compounds in regulating the nuclear factor kappa B and major chemo-radio resistance pathways, contributing to a better understanding of chemo- and radio-resistance in cancer cells. Furthermore, our research has contributed to the facilitation and validation of scientific tools for the development of standardized therapies using botanical sources.

- 1. Lev-Ari S, Strier L, Kazanov D, Madar-Shapiro L, Dvory-Sobol H, Pinchuk I, Marian B, Lichtenberg D, Arber N. Celecoxib and curcumin synergistically inhibit the growth of colorectal cancer cells.Clin Cancer Res. 2005 Sep 15;11(18):6738-44. doi: 10.1158/1078-0432.CCR-05-0171.
- 2. Lev-Ari S, Starr A, Katz burg S, Berkovich L, Rimmon A, Ben-Yosef R, Earon G, Ron I, Vexler A. Curcumin induces apoptosis and inhibits growth of orthotopic human non-small cell lung cancer xenografts Journal of nutritional biochemistry. 2014 Aug;25(8):843-850.
- 3. Conti S, Vexler A, Edry-Botzer L, Hagoel L, Koren B, Honig N, Shtraus N, Meir Y, Marmor S, Shtabsky A, Earon G, Ron I, Lev-Ari S. Combined acetyl-11-keto-beta-boswellic acid and radiation treatment inhibited glioblastoma tumor cells. PLoS One 2018 Jul 3;13(7): e0198627.
- Lev-Ari S, Starr AN, Vexler A, Kalich-Philosoph L, Yoo H, Kwon K, Yadgar M, Bondar E, Ban-Shai A, Volovitz I, Schwarz Y. Rh2-enriched Korean Ginseng (Ginseng Rh2+) inhibits tumor growth and development of metastasis of non-small cell lung cancer. Food & Function 2021; https://doi.org/10.1039/D1FO00643F0

Complete List of Published Work:

https://pubmed.ncbi.nlm.nih.gov/?term=Lev-Ari+S&cauthor_id=33923661