



## Dr. David Gurwitz, Ph.D.

Department of Human Molecular Genetics and  
Biochemistry, Sackler Faculty of Medicine  
Sagol School of Neuroscience

TEL AVIV UNIVERSITY  
אוניברסיטת תל-אביב



Email: gurwitz@post.tau.ac.il  
URL: [http://neuroscience-web.tau.ac.il/en/?post\\_type=portfolio&p=1757](http://neuroscience-web.tau.ac.il/en/?post_type=portfolio&p=1757)



# Genomic Biomarkers for CNS Drug Response

## Positions

Director, National Laboratory for the Genetics of Israeli Populations

Adjunct Professor, University of Florida, Gainesville, FL, USA

Senior Editor, *Pharmacogenomics*

Editorial Board: *Trends in Molecular Medicine, Genome Medicine, CNS Drugs, Biopreservation and Biobanking, Drug Development Research, Pharmaceutical Biology*

Member of the NIH Pharmacogenomics Research Network (PGRN)

## Research

Our lab, serving as the National Laboratory for the Genetics of Israeli Populations (<http://nlqip.tau.ac.il>), was established in 1995 by the Israeli Academy for Sciences and Humanities as the National Biobank of Israel. The biobank includes DNA samples and immortalized lymphoblastoid cell lines from over 2000 unrelated healthy donors representing the large genetic diversity of Jewish, Arab and Druze communities of Israel. This novel resource has been applied by hundreds of research groups in Israel and abroad.

Our primary interest is in finding genomic biomarkers for the response to CNS drugs – , for improving personalized medicine with respect to both treatment efficacy and safety. Our research is currently focused on drugs for treating major depression, bipolar disorder, and Alzheimer's disease. These CNS diseases inflict huge societal costs, and biomarkers are needed for better treatment. We use human immortalized lymphoblastoid cell lines from unrelated healthy donors for comparing drug response and searching for genomic biomarkers, including mRNA for genes, and non-coding RNAs such as microRNAs (miRNAs) and small nucleolar RNAs (snoRNAs).

Among genes that we identified as tentative genomic biomarkers for the response to anti-depressant drugs, two genes, CHL1 and ITGB3, have been replicated in clinical cohorts of major depression patients, lending support for our novel research approach.

A recent publication from our lab has been cited in a report by Scientific American: Unraveling the Mystery of How Antidepressants Work:

<http://www.scientificamerican.com/article/unraveling-the-mystery-of-ssris-depression/>

In addition to the research on genomic biomarkers, we are involved in research on bioethics and societal aspects of human genomics research.

## Publications

Morag A, Kirchheiner J, Rehavi M, **Gurwitz D**. Human lymphoblastoid cell line panels: novel tools for assessing shared drug pathways. *Pharmacogenomics*. 11:327-340 (2010).

**Gurwitz D**. Pharmacogenetics education: 10 years of experience at Tel Aviv University. *Pharmacogenomics*. 11:647-649 (2010).

**Gurwitz D**, Pirmohamed M. Pharmacogenomics: the importance of accurate phenotypes. *Pharmacogenomics*. 11:469-470 (2010).

Bismuth-Evenzal Y, Roz N, **Gurwitz D**, Rehavi M. N-methyl-citalopram: A quaternary selective serotonin reuptake inhibitor. *Biochem Pharmacol*. 80:1546-1552 (2010).

Donnelly MP, Paschou P, Grigorenko E, **Gurwitz D**, Mehdi SQ, Kajuna SL, Barta C, Kungulilo S, Karoma NJ, Lu RB, Zhukova OV, Kim JJ, Comas D, Siniscalco M, New M, Li P, Li H, Manolopoulos VG, Speed WC, Rajeevan H, Pakstis AJ, Kidd JR, Kidd KK. The distribution and most recent common ancestor of the 17q21 inversion in humans. *Am J Hum Genet*. 86:161-171 (2010).

- Shahin H, Walsh T, Rayyan AA, Lee MK, Higgins J, Dickel D, Lewis K, Thompson J, Baker C, Nord AS, Stray S, **Gurwitz D**, Avraham KB, King MC, Kanaan M. Five novel loci for inherited hearing loss mapped by SNP-based homozygosity profiles in Palestinian families. *Eur J Hum Genet.* 18:407-413 (2010).
- Behar DM, Yunusbayev B, Metspalu M, Metspalu E, Rosset S, Parik J, Rootsi S, Chaubey G, Kutuev I, Yudkovsky G, Khusnutdinova EK, Balanovsky O, Semino O, Pereira L, Comas D, **Gurwitz D**, Bonne-Tamir B, Parfitt T, Hammer MF, Skorecki K, Vilems R. The genome-wide structure of the Jewish people. *Nature.* 466:238-242 (2011).
- Kamal SM, Warnich L, Ferguson LR, Srivastava S, Ray S, Avard D, Joly Y, Le Huynh M, Page M, Masellis M, Dove ES, **Gurwitz D**, Ozdemir V. Forward Look: Tenth Anniversary of the Human Genome Sequence and 21 Century Postgenomics Global Health - A Close Up on Africa and Women's Health. *Curr Pharmacogenomics Person Med.* 9:148-155 (2011).
- Gurwitz D**, Lunshof JE. Personalized participatory medicine: sharing knowledge and uncertainty. *Genome Med.* 3:69 (2011).
- Gurwitz D**. Biomarkers: better donor protection. *Nature.* 470:175 (2011)
- Morag M, Pasmanik-Chor M, Oron-Karni V, Rehavi M, Stingl JC, **Gurwitz D**. Genome-wide expression profiling of human lymphoblastoid cell lines identifies CHL1 as putative SSRI antidepressants response biomarker. *Pharmacogenomics*, 12:171-184 (2011).
- L, Lunshof JE, **Gurwitz D**, Schulte In den Bäumen T, Westerhoff HV, Lange BM, Brand A. Health technology assessment in the era of personalized health care. *Int J Technol Assess Health Care.* 27:118-126 (2011).
- Payne K, **Gurwitz D**. Informing resource allocation decision making: economic evaluations of pharmacogenetic tests. *Drug Dev. Res.* 71:445-448 (2011).
- Oved K, Morag M, Pasmanik-Chor M, Oron-Karni V, Shomron N, Rehavi M, Stingl JC, **Gurwitz D**. Genome-wide expression profiling of human lymphoblastoid cell lines identifies several microRNAs as tentative SSRI antidepressants response biomarkers. *Pharmacogenomics* 13:1129-1139 (2012).
- Vincent M, Oved K, Morag A, Pasmanik-Chor M, Oron-Karni V, Shomron N, **Gurwitz D**. Genome-wide transcriptomic variations of human lymphoblastoid cell lines: insights from pairwise gene expression correlations. *Pharmacogenomics* 13:1893-904 (2012).
- Bismuth-Evenzal Y, Gonopolsky Y, **Gurwitz D**, Iancu I, Weizman A, Rehavi M. Decreased serotonin content and reduced agonist-induced aggregation in platelets of patients chronically medicated with SSRI drugs. *J Affect Disord.* 136:99-103 (2012).
- Donnelly MP, Paschou P, Grigorenko E, **Gurwitz D**, Barta C, Lu RB, Zhukova OV, Kim JJ, Siniscalco M, New M, Li H, Kajuna SL, Manolopoulos VG, Speed WC, Pakstis AJ, Kidd JR, Kidd KK. A global view of the OCA2-HERC2 region and pigmentation. *Hum Genet.* 131:683-696 (2012).
- Lunshof JE, **Gurwitz D**. Pharmacogenomic testing: knowing more, doing better. *Clin Pharmacol Ther.* 91:387-389 (2012).
- van Mulligen EM, Fourrier-Reglat A, **Gurwitz D**, Molokhia M, Nieto A, Trifiro G, Kors JA, Furlong LI. The EU-ADR corpus: Annotated drugs, diseases, targets, and their relationships. *J Biomed Inform.* 45:879-884 (2012).
- Tomková M, Marohnic CC, **Gurwitz D**, Seda O, Masters BS, Martásek P. Identification of six novel P450 oxidoreductase missense variants in Ashkenazi and Moroccan Jewish populations. *Pharmacogenomics.* 13:543-554 (2012).
- Gurwitz D**. High-Quality Phenomics are Crucial for Informative Omics Studies. *Drug Development Research* 73:353-356 (2012).
- Gurwitz D**. Data re-identification: protect the children. *Science.* 339(6123):1033 (2013).
- Lunshof JE, **Gurwitz D**. Parental consent: Guarding children's genetic privacy. *Nature.* 494:430 (2013).
- Morag A, Oved K, **Gurwitz D**. Sex differences in human lymphoblastoid cells sensitivities to antipsychotic drugs. *J Mol Neurosci.* 49:554-8 (2013).
- Gurwitz D**, McLeod HL. Genome-wide studies in pharmacogenomics: harnessing the power of extreme phenotypes. *Pharmacogenomics.* 14:337-339 (2013).
- Gurwitz D**. Expression profiling: a cost-effective biomarker discovery tool for the personal genome era. *Genome Med.* 5:41 (2013).
- Oved K, Morag A, Pasmanik-Chor M, Rehavi M, Shomron N, **Gurwitz D**. Genome-wide expression profiling of human lymphoblastoid cell lines implicates integrin beta-3 in the mode of action of antidepressants. *Transl Psychiatry.* 3:e313 (2013).
- Verhoef TI, Ragia G, de Boer A, Barallon R, Kolovou G, Kolovou V, Konstantinides S, Le Cessie S, Maltezos E, van der Meer FJ, Redekop WK, Remkes M, Rosendaal FR, van Schie RM, Tavridou A, Tziakas

D, Wadelius M, Manolopoulos VG, Maitland-van der Zee AH; EU-PACT Group. A randomized trial of genotype-guided dosing of acenocoumarol and phenprocoumon. *N Engl J Med*. 369:2304-12 (2013).

**Gurwitz D.** Gene drives raise dual-use concerns. *Science*. 345:1010 (2014).

**Gurwitz D.** Computing: Keep files small to curb energy use. *Nature*. 514:305 (2014).

**Gurwitz D.** From transcriptomics to biological networks. *Drug Dev Res*. 75(5):267-70 (2014).

**Gurwitz D.,** Milanese E, Koenig T. Grant application review: the case of transparency. *PLoS Biology*. DOI: 10.1371/journal.pbio.1002010 (2014).

### Grants

2011 – 2014 Pharmacogenomics of Antidepressant Drug Response (PADRE): tentative drug response biomarkers from human lymphoblastoid cells, ERA-NET NEURON. Jointly with Julia Stingle, Alessandro Serretti, Andrzej Pilc.

2014 – 2016 SSRI antidepressants as anti-cancer therapy: role for down-regulation of miR-221 and miR-222, Israel Cancer Research Fund (ICRF). Co-PI: Noam Shomron

2014 – 2018 Deciphering beta-amyloid and tau neurotoxicity: Genome-wide expression profiling for sensitivity biomarkers, Israel Science Foundation. Jointly with Illana Gozes

2014 – 2018 LITHOMICS: Lithium response biomarkers: comparative RNA sequencing of patients' lymphocytes and immortalized lymphoblastoid cell lines for personalized treatment of bipolar disorder, US – Israel Binational Science Foundation (BSF). Jointly with Peter Zandi, Thomas Schulze, Fernando Goes, James Potash, John Kelsoe