

BIOGRAPHICAL SKETCH Principal Investigator

NAME ELIAHU HELDMAN	POSITION TITLE: Professor Emeritus, BGU Chief Scientific Officer, Lauren Sciences LLC		
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
The Hebrew University of Jerusalem, Israel	BSc	1962-1965	Agriculture
Technion, Institute of Technology, Haifa, Israel	Compl studies	1965-1966	Chemistry/Biochem
The Hebrew University of Jerusalem, Israel	MSc	1966-1968	Biochemistry
The City University of New York, USA	PhD	1970-1973	Biochemistry
NIH, NHLBI, USA- Fogarty Fellow	Postdoc	1973-1975	Neurobiology

A. Positions and Honors.

Chief Scientific Officer –Lauren Sciences LLC	2012-present	Drug delivery to the brain
Scientist - NCI-SAIC-Frederick, Maryland	2009-2012	Nanobiology/Drug Delivery/Cancer Research
Professor Emeritus - Ben-Gurion University	2009-present	Drug Delivery
Professor - Ben-Gurion University (BGU)	2000-2009	Neurobiology/drug delivery
CSO - NeuroDerm Ltd	2003-2009	Drug delivery/Parkinson's disease
Medals for winning excellent lecturer at BGU	2002, 2003, 2005, 2007	(Biochemistry and Pharmacology)
Adjunct Professor – USUHS, Bethesda, USA	1998-present	Cell Biology
Director, Cell Biology - V.I Technologies –USA	1997-1999	Cell Biology (on Sabbatical leave from IIBR)
Senior Scientist - Israel Inst. for Biol. Research	1977-1998	Neurobiology/Drug Development
Visiting Scientist - USUHS, Bethesda, USA	1989-1990	Neurobiology
Awarded Excellent achievement in R&D – Israel		
Institute for Biological Research	1986	Neurobiology
Visiting Scientist – NIH, NIDDK, USA	1983-1984	Neurotransmitter release
Senior Staff Fellow – NIH, NINDS, USA	1975-1977	Neurobiology
Research assistance, The Hebrew Univ, Israel	1968-1970	Biochemistry

B. Recent Selected peer-reviewed publications (in chronological order).

Over 100 papers in peer reviewed journals and review articles and chapters in books.

Grinberg S, Linder C, Kolot V, Waner T, Wiesman Z, Shaubi E. and **E. Heldman**. Novel Cationic Amphiphilic Derivatives from Vernonia Oil: Synthesis and Self-Aggregation into Bilayer Vesicles, Nanoparticles and DNA Complexants. *Langmuir* 21(17): 7638-7645, 2005.

Wiesman Z, Dom NB, Sharvit E, Grinberg S, Linder C, **Heldman E**, Zaccai M. Novel cationic vesicle platform derived from vernonia oil for efficient delivery of DNA through plant cuticle membranes. *J Biotechnol.* **130**(1):85-94, 2007.

Saar D, Dadon M, Leibovich M, Sharabani H, Grossman Y, **Heldman E**. Opposing effects on muscarinic acetylcholine receptors in the piriform cortex of odor-trained rats. *Learn Mem.* 2007;14(3):224-228.

Grinberg S, Kolot V, Linder C, Shaubi E, Kas'yanov V, Deckelbaum RJ, **Heldman E**. Synthesis of novel cationic bolaamphiphiles from vernonia oil and their aggregated structures. *Chem Phys Lipids.* **153**(2):85-97, 2008.

Mann L, **Heldman E**, Shaltiel G, Belmaker RH, Agam G. Lithium preferentially inhibits adenylyl cyclase V and VII isoforms. *Int J Neuropsychopharmacol.* 2008;11(4):533-539.

Mann L, **Heldman E**, Bersudsky Y, Vatner SF, Ishikawa Y, Almog O, Belmaker RH, Agam G. Inhibition of specific adenylyl cyclase isoforms by lithium and carbamazepine, but not valproate, may be related to their antidepressant effect. *Bipolar Disord.* 2009 Dec;11(8):885-896.

Puri A, Loomis K, Smith B, Lee JH, Yavlovich A, **Heldman E**, Blumenthal R. Lipid-based nanoparticles as pharmaceutical drug carriers: from concepts to clinic. *Crit Rev Ther Drug Carrier Syst.* 26(6):523-80, 2009.

Grinberg S, Kipnis N, Linder C, Kolot V and **Heldman E**. (2010) Asymmetric bolaamphiphiles from vernonia oil designed for drug delivery. *Eur. J. Lipid Sci. Technol.* 2010, 112, 137–151.

Popov M, Linder C, Deckelbaum RJ, Grinberg S, Hansen IH, Shaubi E, Waner T, **Heldman E**. Cationic vesicles from novel bolaamphiphilic compounds. *J Liposome Res.* 2010 Jun;20(2):147-59.

Shechter Y, **Heldman E**, Sasson K, Bachar T, Popov M and Fridkin M. (2010), Delivery of neuropeptides from the periphery to the brain: Studies with enkephalin. *ACS Chem. Neurosci.* 1:399-406.

Hutter T, Linder C, **Heldman E**, Grinberg S. [Interfacial and self-assembly properties of bolaamphiphilic compounds derived from a multifunctional oil.](#) *J Colloid Interface Sci.* 2012 Jan 1;365(1):53-62.

Popov M, Grinberg S, Linder C, Waner T, Levi-Hevroni B, Deckelbaum RJ, **Heldman E**. [Site-directed decapsulation of bolaamphiphilic vesicles with enzymatic cleavable surface groups.](#) *J Control Release.* 2012 Jun 10;160(2):306-14

Dakwar G, Hammad IA, Popov M, Linder C, Grinberg S, **Heldman E**, Stepensky D. [Delivery of proteins to the brain by bolaamphiphilic nano-sized vesicles.](#) *J Control Release.* 2012 Jun 10;160(2):315-21.

Klein M, Weksler N, Gidron Y, **Heldman E**, Gurski E, Smith OR, Gurman GM. Do waking salivary cortisol levels correlate with

Professor Eliahu Heldman

A Summary of scientific activities and professional experience

Throughout my professional career I have focused on neurobiology, pharmacology and related fields. I completed my PhD studies at the City University of New York in 1973 on the subject of "biochemical consequences of electro convulsive shock". My positions and professional experience since then are summarized in my brief biographical sketch, which is enclosed with this summary.

A more detailed description of my professional experience is described herein:

From 1973-1975 I did my post-doctorate work at the National Institutes of Health in Bethesda Maryland, USA, under the supervision of the Nobel Laureate – Dr. Marshal Nirenberg. The subject of my post-doc work was identification of neurotransmitters and synaptogenesis in neuronal cell lines.

From 1975-1977 I was a Senior Staff Fellow at the National Institutes of Health, working on biochemistry of learning and memory.

From 1977-1998 I served as a Senior Scientist in the Israel Institute for Biological Research, where I was a project leader and in charge of the evaluation of CNS-active drugs under development. Among the project that I worked on was "the development of muscarinic drugs for the treatment of neurological diseases, such as Alzheimer's disease. One of the drugs that we have developed, and of which I am a co-inventor, is EVOXAC® (cevimeline) that has been approved by the FDA and is now used clinically for the treatment of Sjogren's syndrome.

From 1997-1999 I served as a lab director in a biotech company in the USA (V.I. Technologies), where I was in charge of the laboratory of Cell Biology and among other projects of the company, I developed a biological glue for wound closure and healing.

In parallel and until now I hold a position of an Adjunct Professor in the Uniformed Services University of Health Sciences (USUHS) in Bethesda Maryland, USA. Among the projects on which I worked in USUHS was the development of drugs for the treatment of Cystic Fibrosis.

From 2000-2009 I was a full Professor at Ben Gurion University (BGU) of the Negev in Beer Sheva Israel and since then until now I continue to serve as a Professor Emeritus with an active laboratory at BGU. In BGU I am developing a drug delivery system based on nanotechnology. This drug delivery system

was licensed to a Biothech Company in the USA (see below). In BGU I also worked on nicotinic receptors, muscarinic receptors and their involvement in cognitive functions and on the biochemistry and physiology of learning and memory as well as on the development of transdermal delivery system for the treatment of Parkinson's disease.

In 2003 I established a start-up company (NeuroDerm Ltd.) that first operated as an incubator company funded by the Israel Ministry of Commerce. In 2007 NeuroDerm raised its first \$2.5M out of the total of about \$20M which were raised until now and the company moved to the Science Park in Ness Ziona, where NeuroDerm is active today. The company is about to issue an IPO in NASDAQ. From 2003-2009 (until I moved to the NIH, see below) I served as the Chief Scientific Officer of the company and as the founder of the company I was a member of its Board of Directors.

From 2009-2011 I served as a Scientist at the National Institutes of Health, where I continued the development of the nanotechnology-based drug delivery system that I and colleagues have initially developed in Ben Gurion University. The work at the NIH was done under an MTA with Ben Gurion University.

From 2011 – now, in addition of being Professor Emeritus in Ben Gurion University, I am serving as a Chief Scientific Officer of Lauren Sciences LLC in New York, the company that purchased the license for our technology from Ben Gurion University. Currently, Lauren Sciences LLC develops the nanotechnology-based drug delivery system for clinical use. In addition, I am currently serving as the Chief Technology Officer (CTO) of an incubator company – Mental Heal that develops a drug for the treatment of Schizophrenia with funding from the Chief Scientist of the Israeli Minister of Economy.

anesthesiologist's job involvement? *J Clin Monit Comput.* 2012;26(6):407-413.

- Yavlovich A, Viard M, Zhou M, Veenstra TD, Wang JM, Gong W, **Heldman E**, Blumenthal R, Raviv Y. Ectopic ATP synthase facilitates transfer of HIV-1 from antigen-presenting cells to CD4(+) target cells. *Blood.* 2012;120(6):1246-1253.
- Kaufman Y, Grinberg S, Linder C, **Heldman E**, Gilron J, Freger V. Fusion of bolaamphiphile micelles: a method to prepare stable supported biomimetic membranes. *Langmuir.* 2013;29(4):1152-1161.
- Kim T, Afonin KA, Viard M, Koyfman AY, Sparks S, **Heldman E**, Grinberg S, Linder C, Blumenthal RP, Shapiro BA. In Silico, In Vitro, and In Vivo Studies Indicate the Potential Use of Bolaamphiphiles for Therapeutic siRNAs Delivery. *Mol Ther Nucleic Acids.* 2013;2:e80.
- Afonin KA, Viard M, Martins AN, Lockett SJ, Maciag AE, Freed EO, **Heldman E**, Jaeger L, Blumenthal R, Shapiro BA. Activation of different split functionalities on re-association of RNA-DNA hybrids. *Nat Nanotechnol.* 2013;8(4):296-304.
- Philosof-Mazor L, Dakwar GR, Popov M, Kolusheva S, Shames A, Linder C, Greenberg S, **Heldman E**, Stepensky D, Jelinek R. Bolaamphiphilic vesicles encapsulating iron oxide nanoparticles: new vehicles for magnetically targeted drug delivery. *Int J Pharm.* 2013;450(1-2):241-249.
- Popov M, Abu Hammad I, Bachar T, Grinberg S, Linder C, Stepensky D, **Heldman E**. Delivery of analgesic peptides to the brain by nano-sized bolaamphiphilic vesicles made of monolayer membranes. *Eur J Pharm Biopharm.* 2013;85(3 Pt A):381-389.
- Stern A, Guidotti M, Shaubi E, Popov M, Linder C, **Heldman E**, Grinberg S, Steric environment around acetylcholine head groups of bolaamphiphilic nanovesicles influences the release rate of encapsulated compounds. *Int. J. NanoMed* 2014, 9, 561-574

ISSUED PATENTS

- Zabicky J, Linder C, Grinberg S, **Heldman E**: Nano- and mesosized particles comprising an inorganic core, process and applications thereof. US 8,377,469 Issued February 19 2013
- Heldman E**, Linder C, Grinberg S, Kolot V and Shaubi E: Amphiphilic compounds and vesicles/liposomes for Organ-Specific Drug Targetting. US **7887833**, Issued – February 15, 2011.
- Grinberg, S. Linder C., Wiesman Z., Kolot V. and **Heldman E**. [Amphiphilic derivatives for the production of vesicles, micelles and complexants, and precursors.](#) US**7939562**, Issued – May 10, 2011.
- Kushnir M. and Heldman E**. [Apparatus for the transdermal treatment of Parkinson's disease.](#) US**6746688**, Issued - June 8, 2004.
- Fisher A., Grunfeld Y., **Heldman E.**, Karton I., Levy A. [Pharmaceutical composition comprising a spiro oxathiolon/quinuclidine and method of treating senile dementia.](#) Issued – April 21, 1992.
- Fisher A., Grunfeld Y., **Heldman E.**, Karton I., Levy A. [Derivatives of quinuclidine.](#) Issued – August 8, 1989

SELECTED CHAPTERS IN BOOKS

- Heldman E.**, Amir A., Pittel Z., Shahar A. and Fisher A. AF64A-induced cholinotoxicity in rat brain synaptosomes and primary cell culture. In: Cellular and Molecular Basis of Cholinergic Function. (Ed. Dowdall, M.J.), pp. 618-626, Ellis Harwood Publisher, Chichester, Sussex, U.K., 1987.
- Fisher A., Brandeis R., Karton I., Pittel Z., Dachir S., Sapir M., Grunfeld Y., Levy A. and **Heldman E**. AF102B: A novel M1 agonist as a rational treatment strategy in Alzheimer's disease. In: Advances in Behavioral Biology 36, Novel Approaches to the Treatment of Alzheimer's Disease.(Eds. E.M. Meyer, J. Simpkins and J. Yamamoto), pp. 11-16, Plenum Press, New York, 1989.
- Heldman E.**, Zimlichman R., Levine M., Raveh L. and H.B. Pollard. Relationships between catecholamine secretion and distinct calcium fluxes in cultured medullary chromaffin cells. In: Calcium Channels Modulators in Heart and Smooth Muscle: Basic mechanisms and Pharmacological Aspects. (Eds. Abraham S. and Amitai G.), pp. 87-103, Balaban Publishers, VCH, Weinheim, Grmany, 1990.
- Fisher A., **Heldman E.**, Gurwitz D., Haring R., Meshulam H., Brandeis R., Pittel Z., Marciano D., Sapir M., Barak D., Vogel Z. and Karton Y. New M1 agonists: Selective signalling, neurotrophic-like and cognitive effects - implications in the treatment of Alzheimer's disease. In: Alzheimer's and Parkinson's diseases. (I Hanin., Yoshida M. and Fisher A. Eds.) Advances in Behavioral Biology Vol. 44, 449- 455, Plenum Press, New York. 1995.
- Heldman E.**, Pittel Z., Haring R., Eshhar N., Levy R., Vogel Z., Marciano D., Kloog Y. and Fisher A. The molecular basis underlying the discrete activation of signal transduction pathways by selective muscarinic agonists. In: Advances in Behavioral Biology Vol. 49, Progress in Alzheimer's and Parkinson's Disease. Plenum Press (Eds. A. Fisher., M. Yoshida and I. Hanin), pp. 503-508, 1998.

C. Research Support (Recent Grants) P.I. or co P.I. on all grants.

Pharmacologica – DRUGS ADME	Israel Ministry of Commerce – Magnet Program	2001-2002
Tissue-targeted smart surfaced nano-size vesicles	Yeshayahu Horowitz Applied Research Fund	2003-2006
Transdermal delivery systems for treatment of Parkinson's	NeuroDerm Ltd.	2003-2009
Hydrogen-bonding interactions between vesicle forming amphiphiles and vesicle stability	US-Israel Binational Science Foundation	2004-2008
Oral delivery of opioid peptides by novel nano-size vesicles	Israel Ministry of Trade Commerce and Labor	2007-2008
Alleviation of late motor complications of PD	Michael J Fox Foundation, USA	2005-2009
BBB permeability of bolavesicles	Israel Science Foundation	2011-present
Targeted Delivery of GDNF to brain	Michael J. Fox Foundation	2011-2012
Targeted Delivery of GDNF to brain	Michael J. Fox Foundation	2012-2014
Delivery of Tenofovir to the Brain	The Campbell Foundation	2012- 2013
Targeted Delivery of GDNF to Brain Motoneurons	ALS Association	2014-present

BIOGRAPHICAL SKETCH-Co P.I.

NAME	POSITION TITLE
CHARLES LINDER	Research Professor, BGU Director of Biophysics, Lauren Sciences

EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE (<i>if applicable</i>)	YEAR(s)	FIELD OF STUDY
Brooklyn College	MSc	1965-1967	Organic chemistry
Polytechnic Institute of Brooklyn	PhD	1967-1972	Polymers, Macromolecules and physical chemistry

A. Positions and Honors.

Ben-Gurion University	1998-present	Research Professor Supramolecular chem., nanovesicles, membr.
Membrane Products Kiryat Weizmann	1976-1998	R&D Manager-Membrane developments, drug delivery
Hoffman LaRoche	1972-1976	Senior Scientist Drug Delivery
Award: The Weizmann Institute of Science: H. Dudley Wright Achievement Prize "For Contribution of Membrane Research to the Greater Good of Mankind"		

B. Selected peer-reviewed publications of last 10 years.

<p>1) Stern A, Guidotti M, Shaubi E, Popov M, Linder C, Heldman E, Grinberg S, Steric environment around acetylcholine head groups of bolaamphiphilic nanovesicles influences the release rate of encapsulated compounds. <i>Int. J. NanoMed</i> 2014, 9, 561-574</p> <p>2) Popov M, Abu Hammad I, Bachar T, Grinberg S, Linder C, Stepensky D, Heldman E. Delivery of analgesic peptides to the brain by nano-sized bolaamphiphilic vesicles made of monolayer membranes. <i>Eur J Pharm Biopharm.</i> 2013 Nov; 85 (3 Pt A): 381-9</p> <p>3) Philosof-Mazor L, Dakwar GR, Popov M, Kolusheva S, Shames A, Linder C, Greenberg S, Heldman E, Stepensky D, Jelinek R. (2013) Bolaamphiphilic vesicles encapsulating iron oxide nanoparticles: New vehicles for magnetically targeted drug delivery. <i>Int J Pharm.</i> Apr 24;450(1-2):241-249.</p> <p>4) Kim T, Afonin K, Viard M, Koyfman A, Sparks S, Heldman E, Grinberg S, Linder C, Blumenthal R and Shapiro B (2013) <i>In silico, in vitro</i> and <i>in vivo</i> studies indicate the potential use of bolaamphiphiles for therapeutic siRNA delivery, <i>Nature Therap Nuc Acids</i> March; 2(3): e80</p> <p>5) T. Hutter T., Linder C, Heldman E., and Grinberg S., Interfacial and self-assembly properties of bolaamphiphilic compounds derived from a multifunctional oil, <i>Journal of Colloid and Interface Science</i>, 365(1), p 53-62, 2012.</p> <p>6) Popov M, Grinberg S, Linder C, Bachar Z, Waner T, Deckelbaum R and Heldman E (2012) Site-directed decapsulation of bolaamphiphilic vesicles with enzymatic cleavable surface groups. <i>J. Controlled Release</i>, Jun 10;160(2):306-14, 2012</p> <p>7) Dakwar, G, Abu Hammad I, Popov M, Linder C, Grinberg S, Heldman E, Stepensky D (2012) Delivery of proteins to the brain by bolaamphiphilic nano-sized vesicles. <i>J. Controlled Release</i>, 2012 Jun 10;160(2):315-21</p> <p>8) Grinberg S., Kipnis N., Linder C., Kolot V. and Heldman E. Asymmetric bolaamphiphiles from vernonia oil designed for drug delivery. <i>Eur. J. Lipid Sci. Technol.</i> 112: 137–151, 2010</p> <p>9) Popov M., Linder C., Deckelbaum R.J., Grinberg S., Hansen I.H., Shaubi E., Waner T., Heldman E. Cationic vesicles from novel bolaamphiphilic compounds. <i>J Liposome Res</i>;20(2):147-59, 2010</p> <p>10) Grinberg S, Kolot V, Linder C, Shaubi E, Kas'yanov V, Deckelbaum RJ, Heldman E. Synthesis of novel cationic bolaamphiphiles from vernonia oil and their aggregated structures. <i>Chem Phys Lipids.</i> 153(2): 85-97, 2008.</p> <p>11) Wiesman Z, Dom NB, Sharvit E, Grinberg S, Linder C, Heldman E, Zaccai M. Novel cationic vesicle platform</p>
--

derived from vernonia oil for efficient delivery of DNA through plant cuticle membranes. *J Biotechnol.* 130(1):85- 94, 2007

12) **Charles Linder** and Ora Kedem , “History of Nanofiltration from 1960 to 1990’s”, First chapter in the book *Nanofiltration- Principles and Applications*, editors A. I. Schaefer, A.G. Fane and T. D. Waite, 12) A. Markus and **C Linder** , "Advances in the technology of controlled release pesticide formulations" in *Microencapsulation: Methods and Industrial Applications* , S. Benita (Ed), pages 45 publishers Taylor and Francis Group LLC, published in 2006

13) S. Grinberg, **C. Linder**, V. Kolot, T. Waner, Z. Wiesman, E. Shaubi, and E. Heldman "Novel Cationic Amphiphilic Derivatives from Vernonia Oil: Synthesis and Self-Aggregation into Bilayer Vesicles, Nanoparticles, and DNA Complexants" *Langmuir*; 21(17) pp 7638 – 7645, 2005

14) Oren, Y., Freger, V. and **Linder, C.**, 2004: Highly ordered heterogeneous ion exchange membranes. *Journal of Membrane Science* 239(1), 17-26. (2004)

15) Y. Oren, I. Rubinstein, **C. Linder**, G. Saveliev, B. Saltzman, E. Mirsky, O Kedem, “Modified Heterogenous Anion Exchange Membranes for Desalination of Brackish and Recycled Water” *Environmental Engineering Science*, 19(6), 512, 2003

16) I. Rubinstein, B. Zaltzman, J. Peretz and **C Linder**, “Experimental verification of the electro-osmotic mechanism of overlimiting conductance through a cation exchange membrane” *Journal of Russian Electrochemistry (Translation of Elektrokimiya)*, 38(8) 653-863, 2002.

17) **C. Linder** and Ora Kedem “ Asymmetric ion exchange mosaic membranes with unique selectivity” *Journal of Membrane Science* 181 , 39-56, 2001

Patents-Issued and Relevant to project

Zabicky J, **Linder C**, *Grinberg S* , *Heldman E*: Nano- and mesosized particles comprising an inorganic core, process and applications thereof . US 8,377,469 Issued February 19 2013

Heldman E, **Linder C**, Grinberg S, Kolot V and Shaubi E: Amphiphilic compounds and vesicles/liposomes for Organ-Specific Drug Targetting. US **7887833** , Issued – February 15, 2011.

Grinberg, S. **Linder C.**, Wiesman Z., Kolot V. and Heldman E. [Amphiphilic derivatives for the production of vesicles, micelles and complexants, and precursors.](#) US**7939562**, Issued – May 10, 2011.

C. Research Support. P.I. or co P.I. on all grants

Recycling Chemicals, Energy and Water from Aggressive Waste Water Streams with Novel Modified Nanofiltration (NF) Membranes	European Consortium project (RENOMEN)	2001-2004
Hydrogen-bonding interactions between vesicle forming amphiphiles and vesicle stability	US-Israel Binational Science Foundation	2004-2008
Tissue-targeted smart surfaced nano-size vesicles	Yeshayahu Horowitz Applied Research Fund	2002-2004
Oral delivery of opioid peptides by novel nano-size vesicles	Israel Ministry of Trade Commerce and Labor	2007-2008
Development of novel systems For water purification	European Consortium	2009-2011
BBB permeability of bolavesicles	Israel Science Foundation	2011-present
Targeted Delivery of GDNF to brain	Michael J. Fox Foundation	2011-2012
Targeted Delivery of GDNF to brain	Michael J. Fox Foundation	2012-2014
Delivery of Tenofovir to the Brain	The Campbell Foundation	2012- 2013
Targeted Delivery of GDNF to Brain Motoneurons	ALS Assocation	2014-present

BIOGRAPHICAL SKETCH-Co P.I.

NAME SARINA GRINBERG	POSITION TITLE Research Professor, BGU Director of Chemistry, Lauren Sciences		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
The Hebrew University of Jerusalem	BSc	1966-1969	Chemistry
The Hebrew University of Jerusalem	MSc	1970-1972	Organic Chemistry
Weizmann Institute	PhD	1975-1981	Chemistry Organic Chemistry

A. Positions and Honors.

Ben-Gurion University, Department of Chemistry	2005-present	Synthetic organic chemistry, Green chemistry,
Ben-Gurion University, The Institutes for Applied Research	1980-2005	Organic chemistry
Texas A&M University	1988-1989	Polymer Chemistry
" Marsha and Tzvi Shariv Prize for Excellency " awarded by Makhteshim Ltd. and The Institutes for Applied Research, Ben-Gurion University of the Negev, for work in organic chemical synthesis.		

B. Selected peer-reviewed publications (in chronological order).

- S. Bittner, **S. Grinberg** and I. Karton. A novel variation of the Lossen rearrangement. *Tetrahedron Lett.*, 1974, 1965.
- S. Bittner and **S. Grinberg**. Alkylation, acylation and Beckman rearrangement of oximes in the presence of an oxidation-reduction system. *J.C.S. Perkin Trans. I*, 1976, 1708.
- A. Galun, E. Shaubi, A. Markus, **S. Grinberg** and J. Zabicky. Photosensitized cis-trans isomerization of jojoba wax. *JAACS*, **61**, 102-103, 1984
- A. Galun, **S. Grinberg**, A. Kampf and E. Shaubi. Oxidation and halogenation of jojobawax. *JOACS*, **61**, 1088, 1984.
- A. Kampf, **S. Grinberg** and A. Galun. Oxidative stability of jojoba wax. *JAACS*, **63**, 246, 1986.
- S. Grinberg** and E. Shaubi. A simple and rapid method for determination of guayule rubber. *Rubber Chem. Techn.* **59**, 204-207, 1986.
- S. Grinberg** and E. Shaubi. Catalytic activity of PEG-quat phase transfer catalysts in dehydrohalogenation reactions. *Tetrahedron*, **47**, 2895-2902, 1991.
- S. Grinberg** V. Kolot and D. Mills. New chemical derivatives based on *Vernonia galamensis* oil. *Industrial Crops and Products*, **3**, 113-119, 1994.
- S. Grinberg and V. Kas'yanov Soluble polymer-bound phase-transfer catalysts. *Reactive and Functional Polymers* 3453 1997.
- C.K. Mambo, P.M. Gitu, B.M. Bhatt, J. Chweya, **S. Grinberg**, and D. Mills. Synthesis of vernolamides containing tertiary amino groups from *Vernonia galamensis* oil and their biological activities. *Bull. Chem. Soc. Ethiop.* 12(2), 121-128, 1998.
- A. K. Machocho, Paul C. Kiprono, **S. Grinberg**, S. Bittner. Pentacyclic Triterpenoids from *Embelia schimperi* *Phytochemistry*, **62**, 573-577, 2003
- A. K. Machocho, T. Win, **S. Grinberg** and S. Bittner. Reaction of benzoquinones and naphthoquinones with 1,8-diamino-3,6-dioxanonane and with 1,11-diamino-3,6,9-trioxaundecane *Tetrahedron Lett.*, **44**, 5531-5534, 2003
- V. Kolot and **S. Grinberg**. Vernonia Oil Based Acrylate and Methacrylate Polymers and Interpenetrating Polymer Networks Vernonia oil-based acrylate and methacrylate polymers and interpenetrating polymer networks with epoxy resins. *Journal of Applied Polymer Science*, **91**(6), 3835-3843, 2004
- S. Grinberg**, C. Linder, V. Kolot, T. Waner, Z. Wiesman, E. Shaubi and E. Heldman, Novel Cationic Amphiphilic Derivatives from Vernonia Oil: Synthesis and Self-Aggregation into Bilayer Vesicles, *Langmuir*, **21**, 7638-7645, 2005
- Wiesman Z, Dom NB, Sharvit E, **Grinberg S**, Linder C, Heldman E, Zaccai M. Novel cationic vesicle platform derived from vernonia oil for efficient delivery of DNA through plant cuticle membranes. *J Biotechnol.* 130(1):85-94, 2007.

Grinberg S, Kolot V, Linder C, Shaubi E, Kas'yanov V, Deckelbaum RJ, Heldman E. Synthesis of novel cationic bolaamphiphiles from vernonia oil and their aggregated structures. *Chem Phys Lipids*. 153(2): 85-97, 2008.

Guidotti M, Psaro R, Ravasio N, Sgobba M, Gianotti E, and **Grinberg S**. Titanium- Silica catalysts for the production of fully epoxidized fatty acid methyl esters. *Catalysis Letters* **122** (1-2), 53-56, 2008

Grinberg S., Kipnis N., Linder C., Kolot V. and Heldman E. Asymmetric bolaamphiphiles from vernonia oil designed for drug delivery. *Eur. J. Lipid Sci. Technol.* 112: 137–151, 2010

Popov M., Linder C., Deckelbaum R.J., **Grinberg S.**, Hansen I.H., Shaubi E., Waner T., Heldman E. Cationic vesicles from novel bolaamphiphilic compounds. *J Liposome Res*;20(2):147-59, 2010

S. Grinberg, N. Kipnis, C. Linder, V. Kolot and E. Heldman, Asymmetric bolaamphiphiles from vernonia oil designed for drug delivery. *Eur. J. Lipid Sci. Technol.* 112, 137 – 151, 2010.

M. Popov, **S. Grinberg**, C. Linder, Z. Bachar, T. Waner, R. Deckelbaum and E. Heldman Site-directed decapsulation of bolaamphiphilic vesicles with enzymatic cleavable surface groups, *J. Control. Release* , 2012 Jun 10;160(2):306-14

T. Hutter, C. Linder, E. Heldman and **S. Grinberg**, Interfacial and self-assembly properties of bolaamphiphilic compounds derived from a multifunctional oil, *J. Colloid Interface Sci.* **365**, 53-62, 2012.

G. R. Dakwar, I. Abu Hammad, M. Popov, C. Linder, **S. Grinberg**, E. Heldman and D. Stepensky Bolaamphiphilic nanovesicles for the delivery of proteins to the brain, *J. Control. Release*. 2012 Jun 10;160(2):315-21.

Philosof-Mazor L, Dakwar GR, Popov M, Kolusheva S, Shames A, Linder C, **Greenberg S**, Heldman E, Stepensky D, Jelinek R. (2013) Bolaamphiphilic vesicles encapsulating iron oxide nanoparticles: New vehicles for magnetically targeted drug delivery. *Int J Pharm.* Apr 24;450(1-2):241-249.

Popov M, Abu Hammad I, Bachar T, **Grinberg S**, Linder C, Stepensky D, Heldman E. Delivery of analgesic peptides to the brain by nano-sized bolaamphiphilic vesicles made of monolayer membranes. *Eur J Pharm Biopharm.* 2013 Nov; 85 (3 Pt A): 381-9

Stern A, Guidotti M, Shaubi E, Popov M, Linder C, Heldman E, **Grinberg S**, Steric environment around acetylcholine head groups of bolaamphiphilic nanovesicles influences the release rate of encapsulated compounds. *Int. J. NanoMed* 2014, 9, 561-574

Kaufman Y, **Grinberg S**, Linder C, Heldman E, Gilron J, Shen Y, Kumar and M, Freger V. (2014) Supported Bolaamphiphile Membranes for Water Filtration: Role of Lipid-Support Interactions. *J Memb. Sci.* in press.

Chapters in Collective Volumes

J. Zabicky, and **S. Grinberg**, Analytical aspects of organogermanium compounds. In: Patai E., ed. The Chemistry of Organic Germanium, Tin and Lead Compounds. Chichester: John Wiley & Sons Ltd.; 1995: p. 339-363.

J. Zabicky and **S. Grinberg**, Analytical aspects of organolead compounds. In: Patai E. ed. The Chemistry of Organic Germanium, Tin and Lead Compounds. Chichester: John Wiley & Sons Ltd.; 1995: p. 429-451

J. Zabicky, and **S. Grinberg**, Analytical aspects of organotin compounds. In: Patai E., ed. The Chemistry of Organic Germanium, Tin and Lead Compounds. Chichester: John Wiley & Sons Ltd.; 1995: p. 365-427.

J. Zabicky and **S. Grinberg** Analytical aspects of compounds containing the azo, azoxy and hydrazino functional groups, In: Patai E., ed. Chichester: John Wiley & Sons Ltd.; 1997 : p 225-269

Patents

- S. Grinberg**, C. Linder, V. Kolot and Z. Wiesman and E. Heldman: Preparation of fatty acid amphiphilic derivatives for the production of vesicles, micelles and complexants. PCT Int. Appl. (2002), 126 pp. WO 200205501
- E. Heldman, C. Linder, **S. Grinberg**, V. Kolot and E. Shaubi: Amphiphilic compounds and vesicles/liposomes for Organ -specific Drug Targetting PCT Int. Appl. (2003), 90 pp WO 2003047499 A2 20030612
- J. Zabicky, C. Linder, **S. Grinberg**, E. Heldman, Nano- and mesosized particles comprising an inorganic core. PCT Int. Appl. (2006)

C. Research Support. P.I. or co-P.I. on all grants

Hydrogen-bonding interactions between vesicle forming amphiphiles and vesicle stability	US-Israel Binational Science Foundation	2004-2008
Tissue-targeted smart surfaced nano-size vesicles	Yeshayahu Horowitz Applied Research Fund	2002-2004
Oral delivery of opioid peptides by novel nano-size vesicles	Israel Ministry of Trade Commerce and Labor	2008-2009
New compounds based on jojoba oil	Eden Oil Company	2008-2009
BBB permeability of bolavesicles	Israel Science Foundation	2011-present
Targeted Delivery of GDNF to brain	Michael J. Fox Foundation	2011-2012
Targeted Delivery of GDNF to brain	Michael J. Fox Foundation	2012-2014
Delivery of Tenofovir to the Brain	The Campbell Foundation	2012- 2013
Targeted Delivery of GDNF to Brain Motoneurons	ALS Assocation	2014-present

BIOGRAPHICAL SKETCH-Co P.I.

NAME Irwin J. Hollander		POSITION TITLE Vice President of Research & Development, Lauren Sciences	
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Polytechnic Institute of Brooklyn, Brooklyn, NY	B.S.	1969-1973	Chemistry
M.I.T., Cambridge, MA	M.S.	1973-1976	Chemistry
M.I.T., Cambridge, MA	Ph.D.	1976-1980	Biological Chemistry
Boston U. School Medicine, Boston, MA	postdoc	1980-1982	atherosclerosis

A. Positions and Honors.

RESEARCH AND PROFESSIONAL EXPERIENCE

Aug 2010 – Present: Vice President of Research and Development, Lauren Sciences LLC, New York, NY. Startup biotech company developing drug delivery system in collaboration with Prof. Eli Heldman and his colleagues at Ben-Gurion University of the Negev, Beer Sheva, Israel.

1988 – Dec 2009: Principal Research Scientist, Oncology Research, Wyeth Research. Formerly Medical Research Division, American Cyanamid, Pearl River, NY.
Research in the monoclonal antibody program, conjugating toxic drugs to anti-tumor MoAbs, fragments, and other targeting molecules. Served as the biochemistry portion of a team in establishing conjugation and purification conditions for the development of two conjugates as clinical leads, one of which was approved as Mylotarg. Helped develop new mass spec methodology for protein-drug conjugates. Member of team that developed EGFR kinase inhibitor EKB-569 which led to HKI-272 (neratinib) EGFR-Her-2 inhibitor, currently in clinical trials. Part of small team (led by Director Robert Mallon) that developed two PI3K inhibitors with INDs approved by the FDA in 2009. Member of Design Team in Cyanamid. Chairman of Publication Awards Committee 1995. Department Y2K chairman.

1984 - 1987: Research Biochemist, Department of Immunoinflammatory Diseases Research, Monsanto/G.D. Searle, St. Louis, MO.
Major areas of research were in allergy and rheumatoid arthritis. Worked on monoclonal IgE, a recombinant IL-4, glycosylation of IgG in rheumatoid arthritis, purification of natural saccharides, late phase of allergy factor from rats, and inhibitors of mast cell degranulation.

1983: Research Associate, Massachusetts Institute of Technology, Cambridge, MA.
Research on purification of enzymes involved in beta-lactam production, under the direction of Professor Arnold Demain. Succeeded in purifying penicillin cyclase, the first enzyme in beta-lactam biosynthesis ever purified.

1981 - 1983: Research Biochemist, St. Elizabeth's Hospital, Vascular Laboratory, Boston, MA.
Affiliations:
Member: AACR, ACS, AAAS and NY Academy of Sciences, ChemPharma Professional Assoc.

B. Selected peer-reviewed publications (in chronological order).

author on patents on immunoconjugates and enzyme inhibitors:

1. "Conjugates of Methyltrithio Antitumor Agents and Intermediates for their Synthesis." Philip Ross Hamann, Lois Hinman, Irwin Hollander, Ryan Holcomb, William Hallet, Hwei-Ru Tsou, Martin J. Weiss. (1998) U.S. Patent No. 5,773,001.
2. "Linkers Useful for the Synthesis of Conjugates of Methyltrithio Antitumor Agents." Philip Ross Hamann, Lois Hinman, Irwin Hollander, Ryan Holcomb, William Hallet, Hwei-Ru Tsou, Martin J. Weiss. (1998) U.S. Patent No. 5,767,285.
3. "Eneidyne Derivatives Useful for the Synthesis of Conjugates of Methyltrithio Antitumor Agents." Philip Ross Hamann, Lois Hinman, Irwin Hollander, Ryan Holcomb, William Hallet, Hwei-Ru Tsou, Martin J. Weiss. (1998) U.S. Patent No. 5,739,116.
4. "Methods for the Preparation of Monomeric Calicheamicin Derivative/Carrier Conjugates." Martin P. Kunstmann, Irwin J. Hollander, Philip Hamann, Arthur Kunz. (1998) U.S. Patent No. 5,714,586.
5. "Method for the Preparation of Substantially Monomeric Calicheamicin Derivative/Carrier Conjugates." Martin P. Kunstmann, Irwin Hollander, Philip Hamann. (1998) U.S. Patent No. 5,712,374.
6. "Process for Preparing Conjugates of Methyltrithio Antitumor Agents." Philip Ross Hamann, Lois Hinman, Irwin Hollander, Ryan Holcomb, William Hallet, Hwei-Ru Tsou, and Martin J. Weiss. (1999) U.S. Patent No. 5,877,296.
7. "5-Substituted-3(2H)-furanones useful for inhibition of farnesyl-protein transferase." Semiramis Ayril-Kaloustian, Irwin Hollander, and Ann Aulabaugh. (2004) U.S. Patent No. 6,710,078.
8. Andersen R, Hollander I, Roll DM, Kim SC, Mallon RG, Williams DE, Marion F. "Meroterpenoid inhibitors of

phosphoinositide 3 kinase (PI3K).” Patent WO2006081659A1.

Selected Recent Publications

1. Robert Mallon, Larry R. Feldberg, Judy Lucas, Jay Gibbons, Veronica Soloveva, Inder Chaudhary, Christoph Dehnhardt, Efren Delos Santos, Zecheng Chen, Osvaldo dos Santos, Semiramis Ayril-Kaloustian, Aranapakam Venkatesan, Irwin Hollander. **“Antitumor Efficacy of PKI-587, a Highly Potent Dual PI3K/mTOR Kinase Inhibitor”** *Clinical Cancer Research* 17(10), (2011) 3193-3203.
2. Christoph M. Dehnhardt, Aranapakam M. Venkatesan, Zecheng Chen, Efren Delos-Santos, Semiramis Ayril-Kaloustian, Natasja Brooijmans, Ker Yu, Irwin Hollander, Larry Feldberg, Judy Lucas, Robert Mallon **“Identification of 2-oxatriazines as highly potent pan-PI3K/mTOR dual inhibitors”** *Bioorg Med. Chem. Lett.* 21 (2011) 4773–4778
3. Aranapakam M. Venkatesan, Christoph M. Dehnhardt, Efren Delos Santos, Zecheng Chen, Osvaldo Dos Santos, Semiramis Ayril-Kaloustian, Gulnaz Khafizova, Natasja Brooijmans, Robert Mallon, Irwin Hollander, Larry Feldberg, Judy Lucas, Ker Yu, James Gibbons, Inder Chaudhary and Tarek S. Mansour. **“Bis Morpholino 1,3,5-Triazine Derivatives: Potent, Adenosine-5'-triphosphate-Competitive Phosphatidylinositol-3-kinase / Mammalian Target of Rapamycin Inhibitors: Discovery of PKI-587 a Highly Efficacious Dual Inhibitor”** *J. Med. Chem* 53 (2010) 2636–2645
4. Robert Mallon, Irwin Hollander, Larry Feldberg, Judy Lucas, Veronica Soloveva, Aranapakam Venkatesan, Christoph Dehnhardt, Efren Delos Santos, Zecheng Chen, Osvaldo dos Santos, Semiramis Ayril-Kaloustian, and Jay Gibbons. **“Antitumor Efficacy Profile of PKI-402, a dual PI3K/mTOR inhibitor.”** *Molecular Cancer Ther.* 9 (2010) 976-984
5. Chen Z., Aranapakam M. Venkatesan, Christoph M. Dehnhardt, Semiramis Ayril-Kaloustian, Natasja Brooijmans, Robert Mallon, Larry Feldberg, Irwin Hollander, Judy Lucas, Ker Yu, and Tarek S. Mansour. **“Synthesis and SAR of Novel 4-Morpholino-Pyrrolopyrimidine Derivatives as Potent PI3 Kinase Inhibitors.”** *J. Med Chem* 53 (2010) 3169–3182
6. C. M. Dehnhardt, A. M. Venkatesan, E. Delos Santos, Z. Chen, O. Santos, S. Ayril-Kaloustian, N. Brooijmans, R. Mallon, I. Hollander, L. Feldberg, J. Lucas, I. Chaudhary, K. Yu, J. Gibbons, R. Abraham, and T. S. Mansour. **“Lead optimization of N-3-substituted-7-morpholino-triazolopyrimidines as dual PI3K/mTOR Inhibitors: Discovery of PKI-402.”** *J. Med. Chem* 53 (2010) 798–810
7. Nan Zhang, Semiramis Ayril-Kaloustian, James T. Anderson, Thai Nguyen^a, Sasmita Das, Aranapakam M. Venkatesan, Natasja Brooijmans, Judy Lucas, Ker Yu, Irwin Hollander and Robert Mallon **“5-Ureidobenzofuranone indoles as potent and efficacious inhibitors of PI3 kinase- α and mTOR for the treatment of breast cancer”** *Bioorganic & Medicinal Chemistry Letters* 20 (2010) 3526-3529
8. Venkatesan, A.M., Dehnhardt, C.M., Chen, Z., Delos Santos, E., Dos Santos, O., Bursavich, M., Gilbert, A.M., Ellingboe, J.W., Ayril-Kaloustian, A., Khafizova, G., Brooijmans, N., Mallon, R., Hollander, I., Feldberg, L., Lucas, J., Yu, K., Gibbons, J., Abraham, R., Mansour, T.S. **“Novel Imidazolopyrimidines as Dual PI3-Kinase/mTOR Inhibitors.”** *Bioorganic & Medicinal Chemistry Letters* 20 (2010) 653-656
9. David E. Williams, Irwin Hollander, Larry Feldberg, Eileen Frommer, Robert Mallon, Akbar Tahir, Rob van Soest, and Raymond J. Andersen. **“Scalarane-Based Sesterterpenoid RCE-Protease Inhibitors Isolated from the Indonesian Marine Sponge *Carteriospongia foliascens*.”** *J. Natural Products* 72 (2009) 1106-1129.
10. Hollander I., Kunz A., Hamann P.R. **“Selection of reaction additives used in the preparation of monomeric antibody-calicheamicin conjugates.”** *Bioconjugate Chemistry* 19(1) (2008) 358-361.
11. Zask A., Kaplan J., Toral-Barza L., Hollander I., Young M., Tischler M., Gaydos C., Cinque M., Lucas J., Yu K. **“Synthesis and structure-activity relationships of ring-opened 17-hydroxywortmannins: Potent phosphoinositide 3-kinase inhibitors with improved properties and anticancer efficacy.”** *J. Med. Chem* 51(5) (2008) 1319-1323.
12. Kyle S. Craig, David E. Williams, Irwin Hollander, Eileen Frommer, Robert Mallon, Karen Collins, Donald Wojciechowicz, Akbar Tahir, Rob Van Soest, and Raymond J. Andersen. **“Novel sesterterpenoid and norseseterterpenoid RCE-protease inhibitors isolated from the marine sponge *Hippospongia* sp.”** *Tetrahedron Letters* 43, no. 27 (1 July 2002): 4801-4804.
13. P R. Hamann, L M. Hinman, I Hollander, C F. Beyer, D Lindh, R Holcomb, W Hallett, H-R Tsou, J Upeslaci, D Shochat, A Mountain, D A. Flowers, and Irwin Bernstein. **“Gemtuzumab Ozogamicin, A Potent and Selective Anti-CD33 Antibody-Calicheamicin Conjugate for Treatment of Acute Myeloid Leukemia.”** *Bioconjugate Chemistry* 13 (2002): 47-58.
14. S. Wolfe, I.J. Hollander, A.L. Demain. **“Enzymatic Synthesis of a Sulfur-Analog of Penicillin Using the “Cyclase” of *Cephalosporium Acremonium*.”** *Bio/Technology* 2, no. 7 (1984): 635-636.
15. I. Hollander, Y.Q. Shen, J. Heim, A.L. Demain, S. Wolfe. **“A Pure Enzyme Catalyzing Penicillin Biosynthesis.”** *Science* 224 (1984): 610-612.

C. Research Support. co-P.I. on all grants

Targeted Delivery of GDNF to brain	Michael J. Fox Foundation	2011-2012
Targeted Delivery of GDNF to brain	Michael J. Fox Foundation	2012-2014
Delivery of Tenofovir to the Brain	The Campbell Foundation	2012- 2013
Targeted Delivery of GDNF to Brain Motoneurons	ALS Association	2014-present