Alexander Binshtok, PhD, CURRICULUM VITAE

Date Updated: February 5th, 2019

1. Personal Details

Name: Alexander Binshtok, PhD

Date of Birth December 20, 1971

Country of Birth: Ukraine

Date of Immigration July 20, 1990

Israeli ID 304599517

Marital Status Married

Number of Children 5

Military Service 1996-1999, Israel Defense Forces, Academic Professional Officer - Physical

Therapist

Current Position Associate Professor in Medical Neurobiology, Department of Medical Neurobiology

Institute for Medical Research Israel-Canada and Center for Research on Pain

The Hebrew University Medical School, The Edmond and Lily Safra Center for Brain

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2. Higher Education

1995	BPT summa cum laude	Physical Therapy	Ben-Gurion University of the Negev, Beer Sheva, Israel
2006	PhD with distinction	Neurobiology (Supervisor: Prof. Michael	The Hebrew University of Jerusalem, Jerusalem, Israel

Gutnick)

2006-2007	Postdoctoral Fellowship	Anesthesia & Critical Care (Host: Prof. Clifford Woolf, MD, PhD)	Neural Plasticity Research Group, Mass General Hospital and Harvard Medical School	
2007-2010	Instructor	Anesthesia & Critical Care	Harvard Medical School	

3. Appointments at the Hebrew University

2017-present	Associate Professor in Medical Neurobiology	Department of Medical Neurobiology, Field : Neuroscience, Pain Research	The Faculty of Medicine; The Edmond and Lily Safra Center for Brain Sciences, The Hebrew University, Jerusalem
May 2017 – January 2019	Jacob and Lena Joels Memorial Foundation Senior Lectureship for Excellence in the Life and Medical Sciences	The Faculty of Medicine, The Hebrew University, Jerusalem	May 2017 - present
2012 - 2017	Faculty, PI	The Edmond and Lily Safra Center for Brain Sciences, Field : Neuroscience, Pain Research	The Hebrew University, Jerusalem
2012 - 2017	Faculty, PI	The Edmond and Lily Safra Center for Brain Sciences, Field : Neuroscience, Pain Research	The Hebrew University, Jerusalem

4. Additional Functions/Tasks at the Hebrew University

2010-2011	Organizer of the Medical Neurobiology Departmental Seminars
2010-present	Examiner of Master and PhD Theses
2010-present	Member of PhD Committee: Moshe Daninos (Prof. Yoel Yaari); Maximillian Peters (Prof. Baruch Minke); Emiliano Cohen (Prof. Millet Treinin); Rebekah Warvick (Prof. Menachem Hanani); Bushra Yasin (Prof. Baruch Minke); Rachel Goryachnik (Prof. Menachem Hanani); Adina Hazan (Dr. Avi Priel); Gilad Noi (Dr. Avi Priel)
2011-precent	Member of the Teaching Committee, Neuroscience Program, The Hebrew University Faculty of Medicine.
2012-2015	Member of Ethic Committee, The Faculty of Medicine, The Hebrew University
2013-2017	Member of the Research Committee, The Faculty of Medicine, The Hebrew University
2014-2016	Course coordinator, Physiology Bet for Pharmacology and Biomedical Science students.

Curriculum Vitae	Alexander Binshtok, PhD
2015-2018	Person in charge of New Neuroscience Curriculum for Medical students, The Faculty of Medicine, The Hebrew University
2016-2017	Course coordinator, Human Physiology course for Pharmacology and Biomedical Science students
2016-present	Member of the Hebrew University Committee of the Authority for Research Students (Experimental Sciences)
2016-present	Chair of Graduate Neuroscience Program, The Hebrew University Faculty of Medicine
2016 - present	Member of Teaching Committee, Biomedical Science Program, The Hebrew University Faculty of Medicine
2017-present	Member of Admission Committee for Medical School
2017-present	Tutoring (מורה מלווה) of Dr. Dani Rokni
2017-present	Member of Prize Committee, Faculty of Medicine
2017-present	Member of the Interdisciplinary Equipment Committee, Faculty of Medicine
2017-present	Member of the Committee for the Advanced Studies, Faculty of Medicine
2017-present	Member of Teaching Committee, Faculty of Medicine
2017-present	Head of Undergraduate Neuroscience Program, Biomedical Sciences, The Hebrew University Faculty of Medicine
2019-present	Tutoring (מורה מלווה) of Dr. Shai Sabbah

5. Service in other Academic and Research Institutions

2000-2005	Instructor	Physical Therapy	Recanati School for Community Health Professions, Beer Sheva, Israel
2007-2010	Instructor	Anesthesia & Critical Care	Harvard Medical School, Boston, MA
2013 – present	Visiting Professor	Department of Brain and Cognitive Sciences	Seoul National University, Seoul South Korea

2018-2019 Visiting Professor Department of Cellular and Systems Neurobiology Instituto de Neurociencias, UMH-CSIC, Alicante, Spain

6. Other Activity

A. Membership in Professional Societies

1996-present	Federation of European Neuroscience Societies
2004-2006	Israeli Society of Physiotherapy
2004-present	Society for Neuroscience
2010-present	International Association for the Study of Pain
2010-present	The Israel Society for Physiology & Pharmacology
2011-present	Israeli Pain Association
2013	Alumni, Kavli Frontiers of Science

B. Other Professional Positions

2011-2014	Treasurer	The Israel Society for Physiology & Pharmacology
2011-2013	Scientific Advisory Board	The Special Agency for the Management & Implementation of Research, Technological Development & Innovation Actions, Hellenic Republic Ministry of Education, Lifelong Learning and Religious Affairs
2012-2015	Scientific Committee	Israel Society for Neuroscience
2015-2017	Academic Committee	The Jerusalem Brain Community
2017-present	Academic Committee	Center for Research on Pain, The Hebrew University
2018-present	Scientific Committee	The Israel Society for Physiology & Pharmacology
2018'present	Expert Review Board	ERC Consolidator Grants

C. Organization of Conferences

2011-2014	Organizer of the Annual Meetings of the Israel Society for Physiology & Pharmacology, Maale Hahamisha
2011-2015	Organizer of Magnes Memorial Lecture Series
2013	Organizer and the Moderator of the Clinical Conference, Hadassah Medical Center, Jerusalem, Israel
2015	Organizer of the International Workshop "Axons in the desert", Ein Gedi, Israel
2017	Member of steering committee for organization of retreat of the Institute for Medical Research Israel-Canada
2017	Organizer of the International Symposium "Pain in Jerusalem", Jerusalem, Israel

D. Editorial Activities

2007-present	Reviewer	Journal of Neuroscience
2008-present	Reviewer	Anesthesiology
2008-present	Reviewer	Pain
2008-present	Reviewer	Molecular Pain
2008-present	Reviewer	Neuroscience Letters
2008-present	Reviewer	Neuroscience
2009-present	Reviewer	Journal of Neurophysiology
2011-present	Reviewer	PloS ONE
2011-present	Reviewer	Journal of Biomedical Optics
2011-present	Reviewer	Pain Management
2011-present	Member of Editorial Board	Journal of Neurology and Neurophysiology
2012-present	Reviewer	Journal of Neuroinflammation
2012-present	Reviewer	Journal of Physiology
2012-present	Reviewer	Cell
2012-present	Reviewer	Journal of Visualized Experiments

2012-present	Academic Editor	PloS One
2013-present	Reviewer	EMBO Molecular Medicine
2014 – present	Reviewer	Frontiers in Cellular Neuroscience
2014-present	Reviewer	Journal of Molecular Neuroscience
2014 – present	Reviewer	European Journal of Pain
2016 - present	Reviewer	Journal of Pain
2017 - present	Reviewer	Scientific Reports
2017 - present	Reviewer	Neuropharmacology
2017 - present	Reviewer	Frontiers in Molecular Neuroscience
2017 - present	Reviewer	Frontiers in Neurology
2017 - present	Reviewer	eLife

E. Honors and Prizes

1994	Exemplary Student Award	Recanati School for Community Health Professions
2001-2004, 2006	Best Lecturer Award	Ben-Gurion University of the Negev
2002	Travel Award	Federation of European Neuroscience Societies
2006	The Schlomiuk Prize for excellence in PhD work	The Hebrew University of Jerusalem
2007	MGH Executive Committee for Research – Award	Massachusetts General Hospital
2008	Rita Allen Foundation Scholar Award, Finalist	Rita Allen Foundation, Princeton, NJ
2010	Golda Meir Fellowship Fund Award	The Hebrew University of Jerusalem
2010	Edward and Millicent Carew-Shaw Distinguished Faculty Award	The Hebrew University of Jerusalem
2011	Allon Fellowships for Outstanding Young Researchers	Council for Higher Education, Israel

Curriculum Vitae		Alexander Binshtok, PhD
2012	The Prusiner – Abramsky Research Award in Clinical and Basic Neuroscience	The Hebrew University of Jerusalem
2013	Best Poster Award	Annual Meeting of Israeli Society of Neuroscience
2014	Harvey Granat Award in Neuro - Anesthesia Research	The Faculty of Medicine, The Hebrew University of Jerusalem
2014	Distinguished Teacher Award (Rector)	The Hebrew University of Jerusalem
2014	Best Poster Award	Annual Meeting of Israeli Society of Physiology and Pharmacology
2015	Distinguished Teacher Award (Rector)	The Hebrew University of Jerusalem
2015	Best Poster Award	IBRO Meeting, Rio de Janeiro, Brazil
2016	Innovation Forum Outstanding Visitors Award	Shanghai Jiao Tong University, Shanghai, China
2016	Distinguished Teacher Award (Rector)	The Hebrew University of Jerusalem
2017	Best Poster Award	Annual Meeting of Israeli Society of Neuroscience
2018	Humboldt Research Fellowship for Experienced Researchers.	Alexander von Humboldt Foundation

F. Chairpersonship in National and International Meetings

2011	Annual Meeting of Israeli Society of Physiology and Pharmacology, Session - Detection of sensory stimuli: from the pleasure of light touch to suffering from devastating pain
2012	Annual Meeting of the Israel Society for Neuroscience, Session – Synaptic Mechanisms
2013	Organizer and the Moderator of the Clinical Conference, Hadassah Medical Center, Jerusalem, Israel
2013	Israeli Pain Association, Annual Meeting - From Nociceptor to Clinics, Eilat, Israel2013 Neuroscience meets Neurotechnology International Meeting, Session – Circuitry
2013	Axons in the Desert International Meeting, Session - Ion Channels and Axonal Excitability

Curriculum Vitae	Alexander Binshtok, PhD
2013	ILANIT congress, Session - Molecular, cellular and neuronal network basis of pain, Eilat, Israel
2014	Brain Research at the Molecular and Cellular Level, Jerusalem, Israel.
2014	Israeli Society of Neuroscience Meeting in Eilat, Session - Mechanisms of Synaptic Plasticity.
2014	Israeli Society of Physiology and Pharmacology Meeting, Session - Mechanisms of Pain
2015	FENS Featured Regional Meeting, Session - 'Why was my pain perpetual" Thessaloniki, Greece
2017	6 th Conference of the Mediterranean Neuroscience Society, Session - "Ion Channels: a key factor in neuronal dysfunction", St. Julian, Malta.
2017	Israeli Pain Association Annual Meeting, Session – "From molecule to pain: molecular and cellular determinants of pain"

G. Grant Review Activities

2010-present	Israel Science Foundation	Ad hoc member
2011-present	Hellenic Republic Ministry of Education	Ad hoc Member
2011-present	Israeli Ministry of Science, Life Science Division	Ad hoc member
2014 - present	National Research Foundation of Korea (NRF), South Korea	Ad hoc member
2015 - present	Israeli Cancer Association	Ad hoc member
2018 - present	The NSERC Discovery Program, Canada	Ad hoc member

H. Examiner of M.Sc. and Ph.D. theses

2010-present	The Hebrew University Faculty of Medicine, Department of Medical Neurobiology.
2011-present	Koret School of Veterinary Medicine, The Robert H. Smith Faculty of Agriculture, Food & Environment.
2012-present	Haifa University
2014-present	Bar Ilan University
2015-present	Ben Gurion University

7. Research Grants

2011 -2016	PI	European Research Consul - ERC	391,000USD(p/year); <i>Total:</i> 1,955,000 USD
	Mech	Follow the PAIN: Novel Somatotopically-Based anisms of Detection, Transmission and Perpetuati Neuropathic Pain; #13, #14; #15; #17; #18; #20; #	Integrative Approach to Study on of Nociceptive, Inflammatory
2011 -2015	PI	Marie Curie International Reintegration Grant	26,000 USD (p/year); <i>Total: 130,000 USD</i>
	Title: 7 #11, #	Targeted delivery of charged compounds to selecti 12	vely block pain and cancer. #10,
2011 -2016	PI	Rosetrees Trust	12,400 USD (p/year); <i>Total: 62,000 USD</i>
		Development of novel "natural" drug-delivery syst nd cancer cells.	ems to selectively target
2013 -2018	PI	The DIP (Deutsch-Israelische Projektkooperation)	461,000 USD (p/year); <i>Total: 2,157,000 USD</i>
	Germ Mink	rogrammable molecular nanorobots for treatment ann Co-PI – Dr. Katharina Zimmerman; collaborate, Prof. Yoel Yaari; Prof. Heinz Beck; Prof. Peter #20; #21	ors: Dr. Ido Bachelet, Prof. Baruch
2016 -2018	co-PI	National Network of Excellence in Neuroscience - TEVA	25, 000 USD (p/year) Total: 50,000 USD
		investigating the first human loss of function muta- ve new therapy for inflammatory pain. co-PI's: Pro	*
2017 -2022	PI	Israeli Science Foundation	350,000 NIS (p/year); <i>Total 1,750,000 NIS</i>
	Title: P Termin	ain at its Source: Functional and Molecular Organ	ization of Nociceptive Peripheral
2017 -2020	PI	Rosetrees Trust	13,500 USD (p/year) <i>Total: 45,500 USD</i>
	Title:	Pain Selective Anesthesia without Neurotoxicity	

2017	PI	The Hebrew University	Total: 42,000 USD
	Title: F	Pain Selective Anesthesia without Toxicity	
2017	PI	The Hebrew University, ELSC, Equipment Grant	Total: 80,000 USD
	Title: S	Signal transduction and propagation at the nociceptive po	eripheral terminals
2018-2021	co-PI	ISF Israel-Canada	513,000 NIS (p/year); <i>Total: 1,500,000 NIS</i>
		unctional connectomics of peripheral and central pain ci : Gerald Zamponi, University of Calgary	f f

8. Teaching at the Hebrew University

A. Supervision of Masters and Doctoral Degree Students

<u>Master Degree S</u>	<u>Students</u>	
2010-2012	Sagi Gudes Direct to PhD	
	Peripheral mechanisms of itch detection. Effect of proinchannels. #13	aflammatory cytokines on sodium
2010-2012	Hodaya Leibovich	Direct to PhD
	Effect of proinflammatory cytokines on sodium channel	ls
2013-2014	Robert Goldstein	Direct to PhD
	Programmable molecular nanorobots for treatment of ch	ronic pain and epilepsy
2013-2014	Yaki Caspi	Direct to PhD
	The role of Mitochondrial Ion Transport in Survival of N	Nociceptive Neurons
2014-2015	Omer Barkai	
	Programmable molecular nanorobots for treatment of ch	ronic pain and epilepsy; #14
2017-2018	Yoav Mazor	
	Mechanisms of Chronic Irritated Bowel Syndrome	
2018 – present	Lama Abedalraz	
	Detection and transmission of nociceptive signals by	nerve terminals
2018-present	Debora Gershon	

Functional connectomics of peripheral and central pain circuits

2010-2016 Arik Tzour, Co-supervisor: Prof. Yoel Yaari

Neuro-glial interaction in chronic pain and epilepsy; #17

2013-2018 Hagit Raizel Co-supervisor: Prof. Alberto

Gabizon

Targeted delivery of membrane impermeable drugs to selectively affect cancer cells

2013-present Sagi Gudes Co-supervisor: Prof. Adi Mizrahi

Development of novel somatotopically-based approach to study mechanisms of chronic pain,

#13; #14; #15

2013-present Hodaya Leibovich Co-supervisor: Prof. Avihu Klar

Sprouting of peripheral axons following nerve injury and its relation to neuropathic pain, #17

2014-present Robert Goldstein

Detection and transmission of nociceptive signals by nerve terminals; Awarded by 2015

Hoffman scholarship (35.000 USD); #20; #21

2014-present Yaki Caspi

The role of Mitochondrial Ion Transport in Survival of Nociceptive Neurons; #14; #18; #20;

<u>#22: #23</u>

2015-present Omer Barkai

Mechanism of opioid-induced tolerance; Awarded by 2017 Hoffman scholarship (35.000 USD) Awarded by 2018 BSF Prof Rahamimoff Travel Fellowship (4.000 USD) Awarded by the

best poster Award Annual Meeting of Israeli Society of Neuroscience (2017); Awarded

by the best poster lecture Annual Meeting of Israeli Society of Physilogy and Pharmacology (2018); #17; #20

2017-present Yishai Kushnir

Pain selective anesthesia without side effects

2018 – present Ben Title

Spinal cord Mechanism of Morphine Tolerance

2018 – present Yoav Mazor

Mechanisms of Chronic Irritated Bowel Syndrome

Postdoctoral fellows

2011-2012 Felix Blasl

Targeted delivery of membrane impermeable drugs to selectively affect pain and itch

neurons , #13

2011-present Shlomo Tsuriel

Novel multispectral combinatory technique to study pain pathways. *Awarded by 2012 Lady Davis Fellowship (45.000 USD);* #15

2013-present Ben Katz

Programmable molecular nanorobots for treatment of chronic pain and epilepsy. Awarded by National Network of Excellence in Neuroscience Post-Doctoral Fellowship Award (35.000 USD). Awarded by the Fellowship from Edmond and Lily Safra Center for Brain Sciences; #14

B. Courses Taught

2010-2011	General Physiology – Circulation for 3 rd year Medical Students
	Lecturer, 26 hours
2011-present	"Why was my pain perpetual?" (Yirmiyahu 15:18) Mechanisms of pain perception and perpetuation, <i>Graduate Students (M.Sc. and PhD students)</i>
	Course Organizer and Lecturer, 26 hours
2011-present	Hot topics in physiology of Neuronal Tissues - Course 94868, <i>Graduate Students (M.Sc. and PhD students)</i>
	Course Organizer and Lecturer, 52 hours
2011-present	Neurophysiology – Passive and Active Properties of Excitable Membranes, 3 rd year students of Biomedical Sciences and Graduate Students
	Lecturer, 8 hours
2011-present	Sensory Physiology and Pain, 3 rd year students of Biomedical Sciences and Graduate Students
	Lecturer, 6 hours
2011-2013	General Physiology – Cardiovascular System, 2 nd year nursing and occupational therapy students
	Lecturer, 14 hours
2012-present	Neurophysiology – Passive and Active Properties of Excitable Membranes Sensory Physiology for <i>Ist year Pharmacology students</i>
	Lecturer, 6 hours
2013-present	General Physiology – Cardiovascular System, 2 nd year Pharmacology and Medical Science students
	Course Coordinator, Lecturer, 14 hours

2017

Pain Physiology *for Medical students*, Lecturer 4 hours

List of Publications

Alexander Binshtok, PhD

Date Updated: February 5th, 2019

1. Doctoral Dissertation

Binshtok A.M., Intrinsic and synaptic properties of neurons in the mouse somatosensory cortex.

Supervisor: Prof. Michael Gutnick.

With distinction. Awarded with The Schlomiuk Prize for excellence in PhD work. Published as a book -

Binshtok A.M. Neurons at the Gate. Intrinsic and synaptic properties of the neurons in mouse barrel cortex. LAP - Lambert Academic Publishing AG & Co. KG Dudweiler, 2010. # 1, 2.

2. Books

Binshtok A.M. Neurons at the Gate. Intrinsic and synaptic properties of the neurons in mouse barrel cortex. LAP - Lambert Academic Publishing AG & Co. KG Dudweiler. 2010

3. Books Edited

4. Chapters in Collections

Vered E, **Binshtok AM**. Physical Therapy in Low Back Pain. In: Fluman I., editor Cervical and Low Back Pain. Aurora Group; 2002. p. 41-52 (in Hebrew)

5. Articles

A1. Peer reviewed Publications before last appointment

1. Fleidervish IA^{PI}, **Binshtok AM**^S, Gutnick MJ^{PI}. (1998). Functionally distinct NMDA receptors mediate horizontal connectivity in layer IV of mouse barrel cortex.

Neuron. 21:1055-1065. [IF- 15.982; 4/252 (Q1); cited 107 times]

2. **Binshtok AM**^S, Fleidervish IA^C, Sprengel R^C, Gutnick MJ^{PI}. (2006). NMDA receptors in layer 4 spiny stellate cells of the mouse barrel cortex contain the NR2C subunit. *Journal of Neuroscience*. 26(2):708-715. [*IF-* 6.747; 24/252(O1); cited 61 times]

3. Tegeder I^{PI}, Costigan M^{PI}, Griffin RS^C, Abele A^C, Belfer I^C, Schmidt H^C, Ehnert C^C, Nejim J^C, Marian C, Scholz J^C, Wu T^C, Allchorne A^C, Diatchenko L^C, **Binshtok AM**^C, Goldman D^C, Adolph J^C, Sama S^C, Atlas SJ^C, Carlezon WA^C, Parsegian A^C, Lötsch J^C, Fillingim RB^C, Maixner W^C, Geisslinger G^C, Max MB^C, Woolf CJ^{PI}. (2006). GTP cyclohydrolase and tetrahydrobiopterin regulate pain sensitivity and persistence.

Nature Medicine. 12(11):1269-1277. [IF- 28.054; 1/124(Q1); cited 505 times]

4. Kim DY^{PI}, Carey BW^C, Wang H^C, Ingano LA^C, **Binshtok AM**^C, Wertz MH^C, Pettingell WH^C, He P^C, Lee VM^C, Woolf CJ^C, Kovacs DM^{PI}. (2007). BACE1 regulates voltage-gated sodium channels and neuronal activity.

Nature Cell Biology. 9(7):755-764. [IF- 20.058; 7/185(O1); cited 251 times]

5. **Binshtok AM**^{PI}, Bean BP^{PI}, and Woolf CJ^{PI}. (2007). Inhibition of nociceptors by TRPV1-mediated entry of impermeant sodium channel blockers.

<u>Nature</u>. 449 (7162): 607-611. [IF- 42.351; 5/8539; 1/55(Q1); cited 341 times]. Accompanied by News and Views. Rated "Exceptional" and gained factor of 11.2 by "Faculty of 1000 Medicine" - their second highest ranked research publication of all time. Rated "Exceptional" with factor of 10.4 in "Faculty of 1000 Biology" – all time top 25 ranking

- 6. Gerner P^{PI}, **Binshtok AM^{PI}**, Wang CF^C, Hevelone ND^C, Bean BP^C, Woolf CJ^{PI}, Wang GK^{PI} (2008). Capsaicin combined with local anesthetics preferentially prolongs sensory/nociceptive block in rat sciatic nerve.
 - <u>Anesthesiology</u>, V 109, No 5: 872-878, 2008. [IF- 6.168; 1/29(Q1); cited 52 times]. Accompanied by cover, Accompanied by 2008 in Review—one of the 10 articles high-lightened annually by the Editorial board of Anesthesiology.
- 7. **Binshtok AM**^{PI}, Wang H^C, Zimmermann K^C, Amaya F^C, Vardeh D^C, Shi L^C, Brenner G^C, Ji RRC^C, Bean BP^C, Woolf CJ^{PI}, Samad TA^{PI}. (2008). Nociceptors are interleukin-1β sensors. *Journal of Neuroscience*. 28(52):14062-14073. [IF- 6.747; 24/252(Q1); cited 356 times]. Accompanied by Editorial "This week in Journal"
- 8. **Binshtok** AM*PI, Gerner P*PI, Oh SBC, Puopolo MC, Roberson DPS, Suzuki SC, Herbert TT, Wang CC, Kim DC, Chung GC, Mitani AAC, Wang GKC, Bean BPC, Woolf CJPI. (2009). Coapplication of lidocaine and the permanently charged sodium channel blocker QX-314 produces a long-lasting nociceptive blockade. *co-first authorship

 Anesthesiology, 111: 127-137. [IF- 6.168; 1/29(Q1); cited 78 times]. Accompanied by Editorial View; Accompanied by 2009 in Review—one of the 10 articles high-lightened annually by the Editorial board of Anesthesiology
- 9. Kim HY ^S, Kim K ^S, Li HY ^S, Chung G ^S, Park CK ^S, Kim S ^S, Jung S ^S, Lee MK ^S, Ahn DK ^S, Hwang SJ ^S, Kang Y ^S, **Binshtok AM** ^C, Bean BP ^C, Woolf CJ ^C, Oh SB ^{PI}. (2010). Selectively Targeting Pain in the Trigeminal System.
 - Pain, 150: 29-40. [IF- 5.836; 2/29(Q1); cited 46 times] Accompanied by Editorial View

10. Roberson DP* ^S, **Binshtok AM*** ^{PI}, Blasl F ^C, Bean BP ^C, Woolf CJ ^{PI}. (2011). Targeting of sodium channel blockers into nociceptors to produce long-duration analgesia: a systematic study and review. *co-first authorship

<u>British Journal of Pharmacology</u>, 164:48-58. [IF- 4.99; 21/256(Q1); cited 54 times]. Rated "Exceptional" and gained factor of 10 by "Faculty of 1000 Medicine" - top 2% of published articles in biology and medicine. This work was started in Prof. Woolf's laboratory, the data analysis and the manuscript preparation were performed in my lab at the Hebrew University.

- 11. Zakir HM ^{PI}, Mostafeezur RM ^C, Suzuki A ^C, Suzuki H ^C, Maeda T ^C, Seo K ^C, Yamada Y ^C, Yamamura K ^C, Lev S ^C, **Binshtok AM** ^C, Iwata K ^C, Kitagawa J ^{PI}. (2012). Expression of TRPV1 channels after nerve injury provides an essential delivery tool for neuropathic pain attenuation. *PLoS ONE*, 7(9), e44023. [IF- 3.53; 8/55(Q1); cited 30 times]
- 12. Puopolo M PI. **Binshtok AM** C, Yao G T, Oh. SB C, Woolf, CJ C, Bean BP PI. (2013). Permeation and block of TRPV1 channels by the cationic lidocaine derivative QX-314.

 Journal of Neurophysiology, April 2013, 109(7): 1704-12. [IF- 3.041; 26/81(Q2); cited 45 times]. This work was started in Prof. Bean's laboratory, I helped Dr. Puopolo with the formulation of the question, design of the experiments and manuscript preparation.
- 13. Roberson DP ^S, Gudes S ^S, Sprague J ^S, Patoski HAW ^T, Robson VK ^S, Blasl F ^C, Duan B ^S, Oh SB ^C, Bean BP ^C, Ma Q ^C, **Binshtok AM** ^{PI*}, Woolf CJ ^{PI*}. (2013). Activity dependent silencing reveals functionally distinct itch-generating sensory neurons.

 Nature Neuroscience, 2013 Jul; 16(7):910-8. [IF- 16.095; 5/252(Q1); cited 87 times]; Accompanied with News and Views
- * In this publication I am <u>co-corresponding and co-senior author</u> and my student Sagi Gudes and postdoc Dr. Felix Blasl are among the co-authors
- **14**. Gudes S ^S, Barkai O ^S, Caspi Y ^S, Katz B ^S, Lev S ^T, **Binshtok AM** ^{PI} (2014). The Role of Slow and Persistent TTX-resistant Sodium Currents in Acute Tumor Necrosis Factor α Mediated Increase in Nociceptors Excitability.

Journal of Neurophysiology, 2015 Jan 15; 113(2): 601-19 [IF- 3.041; 26/81(Q2); cited 32 times]

15. Tsuriel S. S, Gudes S. S, Draft RW C, **Binshtok AM** PI*, Lichtman JW PI* (2015). A multispectral labeling technique to map many neighboring axonal projections in the same tissue.

Nature Methods, 2015 June; 12(6):547-52. [IF- 32.072; 1/79(Q1); cited 14 times]

- * In this publication I am <u>co-corresponding and co-senior author</u>, my postdoc Dr. Shlomo Tsuriel is the first author and my PhD Student Sagi Gudes is the second author
- **16.** Stueber T PI, Eberhardt MJS, Hadamitzky C S, Jangra AS, Schenk S, Dick F S, Stoetzer C S, Kistner K S, Reeh PW PI, **Binshtok AM** PI, Leffler A PI (2016). The quaternary lidocaine derivate QX-314 activates and permeates human TRPV1 and TRPA1 to produce inhibition of sodium channels and cytotoxicity. *Anesthesiology*, 2016 May;124(5):1153-65; [*IF- 5.9; 3/31; cited 15 times*]
- 17. Tzour A^S, Leibovich H^S, Barkai O^S, Biala Y^T, Lev S^T, Yaari Y^{PI}, **Binshtok AM** PI (2016). K_V7/M channels as targets for inflammation-induced neuronal hyperexcitability. *Journal of Physiology*, 2017 Feb; 595(3):713-738 [*IF- 4.7; 7/83(Q1); cited 6 times*]; Accompanied with Editorial Perspectives.
- **18.** Nita II^S; Caspi Y^S; Gudes S^S; Fishman D^C; Lev S^T; Hersfinkel M^C; Sekler I^{PI}; **Binshtok AM**^{PI} (2016). Privileged crosstalk between TRPV1 channels and mitochondrial calcium shuttling machinery controls nociception.
 - <u>BBA Molecular Cell Research</u>, 2016 Dec; 1863(12):2868-2880; [IF- 5.12; 49/289(Q1); cited 6 times]
- **19.** Cohn Yakubovich D^S, Eliav U^S, Yalon E^S, Schary Y^S, Sheyn D^C, Cook-Wiens G^C, Sun S^S, McKenna CE^S, Lev S^T, **Binshtok AM**^C, Pelled G^{PI}, Navon G^{PI}, Gazit D^{PI}, Gazit Z^{PI} (2017). Teriparatide attenuates scarring around murine cranial bone allograft via modulation of angiogenesis.

Bone, 2017 Apr; 97:192-200 [IF- 3.7; 38/133(O2), cited 3 times]

In this publication Shava Lev from my lab is involved

- **20.** Barkai O^S, Goldstein R^S, Caspi Y^S, Katz B^T, Lev S^T and **Binshtok AM**^{PI} (2017). The role of Kv7/M potassium channels in controlling ectopic firing in nociceptors.
 - <u>Frontiers in Molecular Neuroscience</u>, 2017 Jun 13; 10:181; [IF- 5.154; 35/256(Q1); cited 2 time]; Accompanied by Cover; Recommended by Faculty of 1000.
- **21.** Goldstein R^S, Katz B^T, Lev S^T, **Binshtok AM** PI (2017). Ultrafast optical recording reveals distinct capsaicin-induced ion dynamics along single nociceptive neurite terminals *in vitro*. *Journal of Biomedical Optics*, 2017 Jul 1:22(7):76010; [*IF- 2.86*; 21/90(Q1)]

22. Stueber T^S, Eberhardt MJ^S, Yaki Caspi^S, Lev S^T, **Binshtok AM^{PI}**, Leffler A^{PI} (2017). Differential cytotoxicity and intracellular calcium-signaling following activation of the calcium-permeable ion channels TRPV1 and TRPA1.

<u>Cell Calcium</u>, in press [IF- 3.7; 82/190(Q2)]

In this publication my student Yaki Caspi and my lab manager Shaya Lev are involved

A2. Peer-reviewed publications since last appointment

23. Gershkovitz M^S, Caspi Y^S, Fainsod-Levi T^S, Katz B^S, Michaeli J^S, Khawaled S^S, Lev S^T, Polyansky L^S, Shaul M^C, Sionov R^S, Cohen-Daniel L^S, Aqeilan R^C, Shaul Y^C, Mori Y^C, Karni R^C, Fridlender Z^C, **Binshtok AM**^C and Granot Z^{PI} (2018). Neutrophil Killing of Disseminated Tumor Cells is Mediated by TRPM2.

<u>Cancer Research</u>; 78(10):2680-2690 [IF- 9.1; 15/217(Q1), cited 4 times]

In this publication we have provided essential physiological experiments dissecting the mechanism of neutrophil action. My student Yaki Caspi is second author, my postdoc Ben Katz and my lab manager Shaya Lev are involved

24. Barkai O^S, Piug S^S, Lev S^T, Title B^S, Katz B^S, Eli-Berchoer L^T, Gutstein H^C, **Binshtok AM^{PI}** (2019). Platelet-derived growth factor activates nociceptive neurons by inhibiting M-current and contributes to inflammatory pain.

Pain, in press [IF-5.836; 2/31 (Anesthesiology); 35/261 (Neuroscience) (O1)]

B1. Invited Reviews and Editorials before last appointment

- **1.** Dib-Hajj SD ^{PI}, **Binshtok AM** ^{PI}, Cummins TR ^{PI}, Jarvis MF ^{PI}, Samad TA ^{PI}, Zimmermann K ^{PI}. (2009). Voltage-gated sodium channels in pain states: role in pathophysiology and targets for treatment.
 - Brain Research Reviews, 60(1): 65-83. [IF- 5.93; 29/252(Q1); cited 131 times]
- **2.** Suzuki S^S, Gerner P PI, Colvin AC S, **Binshtok AM** PI. (2009). C-fiber Selective Peripheral Nerve Blockade. *Invited Review*.
 - The Open Pain Journal, 2:24-9. [IF- data not available; cited 10 times]
- 3. Binshtok AM PI. (2011). Mechanisms of Nociceptive Transduction and Transmission: machinery for pain sensation and tools for selective analgesia. <u>Invited Review</u>.
 <u>International Review of Neurobiology</u>; Volume 97: 143-177. [IF- 2.457; 153/252(Q2); cited 16 times]
- **4.** Ginosar Y PI, **Binshtok AM** PI. (2012). Mechanisms in anesthesia and analgesia: convention, crisis and the shoulders of giants.

Anesthesiology, 117(3):451-3. [IF- 6.168; 1/29(Q1); cited 3 times]

5. Litwick A ^S, Lev S ^T, **Binshtok AM** ^{PI}. (2013). Chronic pain-related remodeling of cerebral cortex - "pain memory": a possible target for treatment of chronic pain.

Pain Management, Jan; 3(1):35-45. [IF- data not available; cited 5 times]

6. Participation in Scientific Conferences, Lectures and Other Activity

A. Keynote/Plenary Lectures

2009	Targeted delivery of charged membrane impermeant compounds to pain-sensing cells	Keynote Speaker ; 3 rd Trigeminal sensory and motor function symposium Karuizawa, Japan
2010 2011	Cytokines and Inflamo-sensation: From Fast Nociception to Slow Inactivation The Itching Line: The Cellular Basis of Itch Detection and Transmission	Keynote Speaker; 4 th Trigeminal sensory and motor function symposium Osaka, Japan Plenary Lecture, "Pathophysiology and Neuromolecular Mechanisms of Pain" Meeting, National Institute for Physiological Sciences, Okazaki, Japan
2013	Pain Selective Anesthesia: Chili, Cocaine and Robots -Novel Routes to the Holy Grail	Keynote Speaker; Pain Rehabilitation Meeting: When Pills and Syringes aren't Enough to Effectively Manage Pain, Tel Hashomer Hospital, Ramat Gan, Israel
2013	The Itching Line: Selective Silencing of Primary Afferents Reveals Two Distinct Itch- Specific Sensory Lines	Keynote Speaker ; 2013 Annual Meeting of Korean Society for Brain and Neural Science, Seoul, South Korea
2015	Colouring Pain: Multispectral labelling of peripheral neurons to map the projections of pain fibres in normal and pathological conditions	Keynote Speaker ; Trigeminal sensory and motor function symposium, Kyushu, Japan
2016	Colouring Neuronal Networks	Keynote Speaker , Awardee of the Er Yi Innovation Forum for Outstanding Visitors; Shanghai Jiao Tong University School of Medicine, Shanghai, China

В.

ae		Alexander Binshtok, Ph
2017	Ionic mechanisms of inflammatory pain	Keynote Speaker , 7th International Conference of Pain Treatment, Prizren – Republic of Kosovo
2017	Painful Path for Pain Selective Anesthesia	Keynote Speaker ; 2017 Annual Meeting of Korean Society of Dental Medicine
2019	From physical therapy to physics of pain: lessons from the clinical practice towards the laboratory	Keynote Speaker ; IX International Congress in Physical therapy, Alicante, Spain
Invited Le	ectures	
2007	Pain-selective anesthesia	Harvard Medical School Department of Neurobiology, Boston, Massachusetts, USA
2007	Pain-selective anesthesia	Second Annual Simches Symposium Richard B. Simches Research Center, Boston, Massachusetts, USA
2007	Pain-selective anesthesia	CombinatoRx - Boston, Massachusetts, USA
2007	Can we conquer pain?	Massachusetts Institute of Technology Department of Brain and Cognitive Science, Boston, Massachusetts, USA
2007	Pain Selective Anesthesia	New Insides into Pain and Stress Mechanisms Meeting, Seoul, South Korea
2007	Nociceptors are interleukin-1β sensors	Seoul National University School of Dentistry, Seoul, South Korea
2008	Nociceptors are cytokine sensors	Neuroscience Center Research Presentations Mass General Hospital, Charlestown, Massachusetts, USA
2008	Blockade of pain sensing neurons by TRPV1-mediated entry of membrane impermeant sodium channel blockers	Marine Biology Lab Seminar Series, Imaging Cluster, MBL, Woods Hole, MD, USA
2008	Voltage-gated sodium channels as targets for pain treatment	Discovery on Target Conference World Trade Center, Boston, Massachusetts, USA
2008	Pain-selective anesthesia	International Spring Research Pain Conference, Grand Cayman
2008	Painful conquest of pain	Nihon University School of Dentistry Department of Physiology, Tokyo, Japan

tae		Alexander Binshtok, Phl
2008	Nociceptors are IL-1β sensors	Osaka University School of Dentistry Department of Physiology, Osaka, Japan
2008	Painful conquest of pain	Ben Gurion University The Zlotowski Center for Neuroscience, Beer Sheva, Israel
2009	Blockade of pain sensing neurons by TRPV1-mediated entry of membrane impermeant sodium channel blockers	Neuroscience Center Research Presentations Mass General Hospital, Charlestown, Massachusetts, USA
2009	Targeted delivery of charged membrane impermeant local anesthetics selectively into nociceptors to produce long-lasting regional analgesia	Grand Rounds, Department of Anesthesia and Critical Care, Mass General Hospital, Boston, Massachusetts, USA
2009	Interleukin 1 beta and sodium channels - from Slow Inactivation to Fast Nociception	Keystone Symposium - The Neurobiology of Pain and Analgesia Santa Fe, New Mexico, USA
2009	Voltage-Gated Sodium Channels as Targets for Pain	Nihon University School of Dentistry Department of Physiology, Tokyo, Japan
2010	Follow the Pain: Using ultrafast imaging to study physiology of nociceptive terminals	Massachusetts Eye and Ear Infirmary, Cornea Faculty, Boston, Massachusetts, USA
2010	Charge and Target! Targeted Delivery of Charged Membrane impermeant Compounds to Selectively Block Pain and Itch - Sensing Neurons	2 nd Workshop in Research and Innovation in Medical Technologies, The Hadassah University Hospital, The Hebrew University, Jerusalem, Israel
2010	Voltage-Gated Sodium Channels as Targets for Pain Treatment	Interdisciplinary Center for Neural Computation, The Hebrew University, Jerusalem, Israel
2010	Painful conquest of Pain: Targeted Delivery to Selectively Block Pain	Department of Physiology, Paracelsus Medical University, Salzburg, Austria
2010	Charge and Target! Targeted Delivery of Charged Membrane impermeant Compounds to Selectively Block Pain	Department of Anesthesia and Critical Care, Hadassah Hospital, Jerusalem, Israel
2010	Voltage-Gated Sodium Channels as Targets for Pain Treatment	Israeli Pain Society Meeting, Eilat

e		Alexander Binshtok, Ph.
2010	Novel approaches in pain treatment	Institute of Pharmacology and Toxicology, Parazelsus Medizinische Privatuniversitat, Salzburg, Austria
2010	TRP channels: The Route of Pain or Path for the Pain release?	Nihon University School of Dentistry Department of Physiology, Tokyo, Japan
2010	Novel approaches in pain treatment	Department of Physical Therapy, Ben Gurion University, Israel
2011	Pain Selective Anesthesia: Chili, Cocaine and Mustache - the Novel Routes to Reach the Holy Grail.	Department of Hematology, Hadassah Hospital, Jerusalem, Israel
2011	Charge and Target! Targeted Delivery of Charged Membrane impermeant Compounds to Selectively Block Pain	Neuroscience Center, University of Helsinki, Finland
2011	Pain Selective Anesthesia: Chili, Cocaine and Mustache - Novel Routes to the Holy Grail	Department of Neurology and Neurological Sciences, Stanford University Medical School, Palo Alto, CA
2011	Selective Anesthesia of Nociceptors: The Magic Analgesic Bullet	22 nd International Congress of the Israel Society of Anesthesiologists, Tel Aviv, Israel
2011	Pain Selective Anesthesia: Chili, Cocaine and Mustache - Novel Routes to the Holy Grail	Department of Cellular and System Neurobiology, Instituto de Neurociencias de Alicante, Spain
		Universidad Miguel Hernandez-CSIC
2011	Pain Selective Anesthesia: Chili, Cocaine and Mustache - Novel Routes to the Holy Grail	From Neurons to Networks in Sensorimotor Learning and Perception Workshop, 20th ISFN Annual Meeting, Eilat, Israel
2011	New Technologies to Understand Chronic Pain	Nihon University School of Dentistry Department of Physiology, Tokyo, Japan
2011	The Itching Line: The Cellular Basis of Itch Detection and Transmission	Niigata University Graduate School for Medical and Dental Sciences, Niigata, Japan
2012	The Cellular Basis of Itch Detection and Transmission	Department of Anesthesia and Critical Care, Hadassah Hospital, Jerusalem, Israel
	2010 2010 2010 2011 2011 2011 2011 2011	2010 Novel approaches in pain treatment 2010 TRP channels: The Route of Pain or Path for the Pain release? 2010 Novel approaches in pain treatment 2011 Pain Selective Anesthesia: Chili, Cocaine and Mustache - the Novel Routes to Reach the Holy Grail. 2011 Charge and Target! Targeted Delivery of Charged Membrane impermeant Compounds to Selectively Block Pain 2011 Pain Selective Anesthesia: Chili, Cocaine and Mustache - Novel Routes to the Holy Grail 2011 Selective Anesthesia of Nociceptors: The Magic Analgesic Bullet 2011 Pain Selective Anesthesia: Chili, Cocaine and Mustache - Novel Routes to the Holy Grail 2011 Pain Selective Anesthesia: Chili, Cocaine and Mustache - Novel Routes to the Holy Grail 2011 Pain Selective Anesthesia: Chili, Cocaine and Mustache - Novel Routes to the Holy Grail 2011 Pain Selective Anesthesia: Chili, Cocaine and Mustache - Novel Routes to the Holy Grail 2011 The Itching Line: The Cellular Basis of Itch Detection and Transmission 2012 The Cellular Basis of Itch Detection

tae		Alexander Binshtok, Phl
2012	"Why was my pain undending?" (Jeremiah 15:18) - Geriatric Pain as an Challenge for Engineers	Annual Meeting of Israeli Society for Medical and Biological Engineering, Afeka Tel Aviv Academic College of Engineering, Tel Aviv, Israel
2012	The Itching Line: The Cellular Basis of Itch Detection and Transmission	Faculties of Medicine of Philipps University, Marburg and the Hebrew University, Jerusalem Joint Neuroscience meeting, Jerusalem, Israel
2012	Cytokines and Sodium Channels - from Slow Inactivation to Fast Nociception	Israel Canada Workshop in Medical Neuroscience, Jerusalem, Israel
2012	Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	Department of Neurobiology, Weitzman Institute of Science, Israel
2012	Follow the Pain: Somatotopically- Based Approach to Study Mechanisms of Detection, Transmission and Perpetuation of Pain	Interdisciplinary Center for Neural Computation, The Edmond and Lilly Safra Center for Brain Sciences, The Hebrew University, Jerusalem, Israel
2013	Follow the Pain: Somatotopically- Based Approach to Study Mechanisms of Detection, Transmission and Perpetuation of Pain	Zlotowski Center for Neuroscience, Ben Gurion University of the Negev, Beer Sheva, Israel
2013	Follow the Pain: Somatotopically- Based Approach to Study Mechanisms of Detection, Transmission and Perpetuation of Pain	Molecular Neuroscience Forum Seminar, Weitzman Institute of Science, Israel
2013	Somatotopically-Based Approach to Study and Target Mechanisms of Detection, Transmission and Perpetuation of Pain	Institut für Physiologie und Pathophysiologie, Friedrich-Alexander Universitat, Erlangen- Nurnberg, Germany
2013	Pain Selective Anesthesia – Novel Routes to the Holy Grail	Organizer and Moderator , Hadassah Medical Center, Jerusalem, Israel

2013	Somatotopically-Based Approach to Study and Target Mechanisms of Detection, Transmission and Perpetuation of Pain	The Gonda Brain Research Center, Bar Ilan University, Israel
2013	Selective Silencing of Primary Afferents Reveals Itch-Specific Sensory Lines	BatSheva Workshop on Spatial Challenges in Neuronal Cell Biology, Lopatie Conference Center, Weizmann Institute of Science, Israel
2013	"Why was my pain undending?" (Jeremiah 15:18) - Physiology and Pathophysiology of Pain	13 th Darom Pain Management Meeting, Ben Gurion University of the Negev and Israeli Association of Pain, Beer Sheva, Israel
2013	Cytokines and Sodium Channels - from Slow Inactivation to Fast Nociception	Department of Neurology, Neuroscience & Regeneration Research Center, Yale School of Medicine, Yale University, New Haven, USA
2013	The Itching Line: Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	2013 Annual Meeting of Korean Society for Brain and Neural Science, Seoul, South Korea
2013	Pain Selective Anesthesia: Chili, Cocaine and Mustache (Robots)- Novel Routes to the Holy Grail	Department of Physiology, School of Dentistry, Seoul National University, Seoul Korea
2013	Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	ILANIT Congress, Eilat, Israel
2013	Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	Department of Anesthesia and Critical Care, Hadassah Hospital, Jerusalem, Israel
2013	Somatotopically-Based Approach to Study and Target Mechanisms of Detection, Transmission and Perpetuation of Pain	Department of Neuroscience, Brown University, Providence, RI
2013	Cytokines and Sodium Channels - from Slow Inactivation to Fast Nociception	Second Binational Italian-Israeli Meeting in Neuroscience, Eilat, Israel

tae		Alexander Binshtok, Phi
2013	Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	1 st Brain Disease Research Center (BDRC) meeting, Jerusalem, Israel
2013	Selective Targeting: Chili, Wasabi and Cannabis - Novel Routes to the Holy Grail	Department of Human Genetics and Biochemistry, Sackler School of Medicine Tel Aviv University, Tel-Aviv
2013	Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	Nihon University School of Dentistry Department of Physiology, Tokyo, Japan
2013	Itching for Relief: Novel approaches to study and treat Itch	Department of Oral Anatomy and Neurobiology, Graduate School of Dentistry, Osaka University, Osaka, Japan
2013	The Itching Line: Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	Department of Physiology and Pharmacology, Sackler School of Medicine Tel Aviv University, Tel-Aviv
2014	The Itching Line: Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	Beijing University-ELSC Joint Symposium
2014	"Why was my pain undending?" (Jeremiah 15:18) - and how can we treat it? Novel ways to study how the nervous system detects, codes and perpetuates pain	School of Veterinary Medicine, Faculty of Agriculture, The Hebrew University, Rehovot, Israel
2014	The Itching Line: Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	First Jerusalem Brain Community (JBC) retreat, Kibbutz Maagan, Israel
2014	"Why was my pain undending?" (Jeremiah 15:18) - and how can we treat it? Novel ways to study how the nervous system detects, codes and perpetuates pain	Department of Brain and Cognitive Science, Seoul National University, Seoul, South Korea

itae		Alexander Binshtok, I
2014	The Itching Line: Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	Neuroscience Center, University of Helsinki, Finland
2014	The Labelled Lines of Itch: Activity-Dependent Silencing of Primary Afferents as a Tool to Reveal Distinct Itch-Generating Sensory Neurons	The 22nd Jerusalem School in Life Sciences on: "Frontiers in Neuroscience"
2014	Coding of Itch: Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	Molecular mechanisms in synaptic transmission, sensory transduction and neurodegeneration Workshop the Hebrew University of Jerusalem, Israel and University Medical Center Gottingen, Germany
2014	Physiology and Pathophysiology of Pain	Einstein in Azza, Hebrew University
2014	Coding of Itch: Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines	Department of Neurobiology, University of Haifa
2014	Selective Targeting: Chili, Wasabi and Cannabis - Novel Routes to the Holy Grail	MD Anderson Anesthesiology & Neuroscience Seminar, MD Anderson Cancer Center, Houston, TX
2015	Colouring Neuronal Networks	Institute for Drug Research, The Hebrew University Medical School
2015	Colouring Labelled Lines: Multispectral Mapping and Activity-Dependent Silencing of Primary Afferents as a Tools to Reveal Distinct Pain and Itch Sensory Lines and to Follow up their Reorganization in Chronic Pain	Meeting of Israeli Society of Physiology and Pharmacology

ue		Alexander Binsniok, Fri.
2015	Colouring Labelled Lines: Multispectral Mapping and Activity-Dependent Silencing of Primary Afferents as a Tools to Reveal Distinct Pain and Itch Sensory Lines and to Follow up their Reorganization in Chronic Pain.	Faculty of Life Science, Bar Ilan University
2015	Colouring Labelled Lines: Multispectral Mapping and TRPV1-mediated Activity- Dependent Silencing of Primary Afferents as a Tools to Reveal Distinct Pain and Itch Sensory Lines	Ion Channels, synapses and neuro-issues, 2015 Sino-Israel Workshop of Neuroscience, Shanghai, China
2015	Coding of pain and itch: Selective silencing of primary afferents reveals two distinct itch-specific sensory lines	FENS Regional Meeting, Thessaloniki, Greece
2015	"Why was my pain undending?" (Jeremiah 15:18) - and how can we treat it?	Faculty Lecture; The Hebrew University Faculty of Medicine, Jerusalem, Israel
2015	Colouring Labelled Lines: Multispectral Mapping and TRPV1-mediated Activity- Dependent Silencing of Primary Afferents as a Tools to Reveal Distinct Pain and Itch Sensory Lines	Department of Anesthesiology, Critical Care and Pain Medicine at Salzburg General Hospital, Paracelsus Medical University, Salzburg, Austria
2015	Neuronal GPS: Mapping axonal projections using multispectral labelling technique	Axons in the desert - International research workshop, Ein Gedi, Israel
2016	Colouring Neuronal Networks	Shanghai Jiao Tong University School of Medicine, Shanghai, China
2016	Novel Mechanisms of Opioid Induced Hyperalgesia	Department of Neurobiology, Weizmann Institute of Science, Israel

iue		Alexander Binsmok, 11
2016	Coloring Labelled Lines: Multispectral Mapping and Activity-Dependent Silencing of Primary Afferents as a Tools to Reveal Distinct Pain and Itch Sensory Lines and to Follow up their Reorganization in Chronic Pain	School of Brain and Cognitive Sciences, Beijing Normal University, Beijing, China
2016	Novel routes for pain selective blockade	Brain and Pain Colloquium, Paris, France
2016	$K_{\rm V}7/M$ channels as targets for inflammation-induced neuronal hyperexcitability	Meeting of Israeli Neuroscience Society, Eilat, Israel
2016	Molecular and Cellular Determinants of Pain and Itch Detection	Joint Hebrew University – Peking University workshop on Neuroscience, Hebrew University,
2017	$K_{\rm V}7/M$ channels as targets for inflammation-induced neuronal hyperexcitability	6 th Conference of the Mediterranean Neuroscience Society, St. Julian, Malta
2017	Coloring Chronic Pain	Pain in Jerusalem Symposium, Jerusalem, Israel
2017	Cellular determinants of pain sensation	21st Annual Meeting of Israel Society of Biological Psychiatry, Kfar Blum, Israel
2017	Painful Path to Pain Selective Anesthesia	Annual Meeting of Israeli Pain Association, Eilat
2017	Selective Silencing of Primary Afferent Neurons for Pain and Itch selective block	Tel HaShomer Hospital, Israel
2017	Ion channels as a targets for inflammation-induced nociceptive excitability	Universitas Miguel Hernandez, Institute for Neuroscience, Alicante, Spain
2017	Neuronal GPS: Mapping axonal projections using multispectral labelling technique	Department für Physiologie und Medizinische Physik, Division für Physiologie, Medizinishe Universitat, Innsbruck, Austria

2017	Neuronal GPS: Mapping axonal projections using multispectral labelling technique	Department of Brain and Cognitive Science, Seoul National University, Seoul, South Korea
2017	Pain at its source: Signal transduction and propagation at the nociceptive peripheral terminals	Annual Meeting of the Israeli Society for Neuroscience, Eilat, Israel
2018	A new spice to the inflammatory soup: the role of PDGF in inflammatory pain	Universitas Miguel Hernandez, Institute for Neuroscience, Alicante, Spain
2018	Pain at its source: Signal transduction and propagation at the nociceptive peripheral terminals	Pain Mechanisms and Therapeutics Conference 3 - 8 June, 2018 Taormina, Sicily
2019	Pain at its source: Signal transduction and propagation at the nociceptive peripheral terminals	Universitas Miguel Hernandez, Institute for Neuroscience, Alicante, Spain

7. Selected Conference Poster Presentations (since last appointment):

- 1. Puopolo M, <u>Binshtok AM</u>, Yao GL, Woolf CJ, Bean BP. Permeation of the lidocaine derivative QX-314 in TRPV1 and TRPA1 channels: Is pore dilation required? Society for Neuroscience. 2010. San Diego, CA.
- 2. Roberson DP, Oh SB, Duan B, Bean BP, Ma Q, <u>Binshtok AM</u>*, Woolf CJ*. The itching Line: Selective Silencing of Primary Afferents Reveals Two Distinct Itch-Specific Sensory Lines. The 14th World Congress on Pain meeting, Milan, 2012. *co-corresponding authors
- 3. Gudes S, <u>Binshtok AM.</u> Proinflammatory cytokines directly activate nociceptors by 38-MAPK-dependent relief of slow inactivation of TTX-resistant sodium channels. The 14th World Congress on Pain meeting, Milan, 2012.
- 4. Roberson DP, Spraque J, Blasl F, Duan B, Bean BP, Ma Q, <u>Binshtok AM</u>, Woolf CJ. Selective silencing of primary afferents reveals separable itch specific sensory lines. Society for Neuroscience. 2012. New Orleans, LA.
- 5. Raziel H, Lev S, Honigman A, <u>Binshtok AM.</u> Targeted delivery of membrane-impermeable cytotoxic compounds via TRP channels into specific cells. 21st ISFN Meeting and the 1st Binational Australian-Israeli Neuroscience Meeting. Journal of Molecular Neuroscience, 2012: Nov, p 95.
- 6. Tzour A, Yaari Y, <u>Binshtok AM</u>. Astrocytic P2Y1 receptors induce the spread of calcium waves from astrocytes to neurons. 21st ISFN Meeting and the 1st Binational Australian-Israeli Neuroscience Meeting. Journal of Molecular Neuroscience, 2012: Nov, p 95. <u>Winner of the Best Poster Award</u>
- 7. Gudes S, Leibovich H, <u>Binshtok AM.</u> Proinflammatory cytokines activate nociceptors by p38-MAPK-dependent relief of slow inactivation of TTX-resistant sodium channels. 21st ISFN Meeting and the 1st Binational Australian-Israeli Neuroscience Meeting. Journal of Molecular Neuroscience, 2012: Nov, p 50.

8. Tsuriel S, Leibovich H, Lichtman JW, <u>Binshtok AM</u>. A new multispectral combinatoric tracing technique enables mass neuronal mapping and reveals two level circuit rearrangement during development. 21st ISFN Meeting and the 1st Binational Australian-Israeli Neuroscience Meeting. Journal of Molecular Neuroscience, 2012: Nov, p 124.

- 9. <u>Binshtok AM.</u> "Why was my pain perpetual...?" (Yirmiyahu 15:18). A Somatotopically-Based Approach to Study and Target Mechanisms of Detection, Transmission and Perpetuation of Pain. First Israeli-American Kavli Frontiers of Science Symposium, Israel Academy of Science and Humanities U.S. National Academy of Sciences, Irvine, California
- 10. <u>Binshtok AM.</u> Cytokines and sodium channels from slow inactivation to fast nociception. 22nd ISFN Meeting and the 2nd Binational Italy-Israel Neuroscience Meeting. Journal of Molecular Neuroscience, 2013: Dec, p 20.
- 11. Goldshtein R., Katz B., <u>Binshtok AM.</u> A novel method for electrical stimulation-driven ion imaging: a model for studying DNA nano-devices which can respond to transmitter release. 22nd ISFN Meeting and the 2nd Binational Italy-Israel Neuroscience Meeting. Journal of Molecular Neuroscience, 2013: Dec, p 124.
- 12. Gudes S., <u>Binshtok AM.</u> Proinflammatory cytokine tumor necrosis factor rapidly relieves voltage dependence of slow inactivation of tetrodotoxin-resistant sodium channels, leading to acute nociceptive hyperexcitability. 22nd ISFN Meeting and the 2nd Binational Italy-Israel Neuroscience Meeting. Journal of Molecular Neuroscience, 2013: Dec, p 57. *Winner of the Best Poster Award*
- 13. Tsuriel S., Leibovich H., Peretz L., <u>Binshtok AM</u>. Detection of neuronal sprouting during the development of neuropathic pain. 22nd ISFN Meeting and the 2nd Binational Italy-Israel Neuroscience Meeting. Journal of Molecular Neuroscience, 2013: Dec, p 76.
- 14. Raizel HI., Lev S., Honigman A., <u>Binshtok AM.</u> Targeting charged cytotoxic compounds selectively into specific cells via TRP channels. 22nd ISFN Meeting and the 2nd Binational Italy-Israel Neuroscience Meeting. Journal of Molecular Neuroscience, 2013: Dec, p 103.
- 15. Tzour A., Yaari Y., <u>Binshtok AM</u>. The proinflammatory agent lipopolysaccharide augments calcium signaling from astrocytes to neurons. 22nd ISFN Meeting and the 2nd Binational Italy-Israel Neuroscience Meeting. Journal of Molecular Neuroscience, 2013: Dec, p 124.
- 16. Nita I. Caspi Y. Sekler I. <u>Binshtok AM</u>. TRPV1 dependent neurotoxicity involves the mitochondrial Na+/Ca2+ exchanger in nociceptors. 22nd ISFN Meeting and the 2nd Binational Italy-Israel Neuroscience Meeting. Journal of Molecular Neuroscience, 2013: Dec, p 94.
- 17. Katz B., Goldshtein R., <u>Binshtok AM.</u> A novel method for electrical stimulation-driven ion imaging: a model for studying DNA nano-devices which can respond to transmitter release. ILANIT congress, 2013
- 18. <u>Binshtok AM.</u> The Itching Line: Selective silencing of primary afferents reveals two distinct itch-specific sensory lines. Experimental Neurobiology, 2013, Volume 22, Number 2, Supplement, p29.
- 19. Goldstein R., Katz B., Lev S., <u>Binshtok AM</u>. A model for studying DNA nano-devices which can respond to transmitter release. 2014 Annual Meeting of the Israeli Society of Physiology and Pharmacology, Maale HaHamisha. *Winner of the Best Poster Award*
- 20. Goldstein R., Katz B., Lev S., <u>Binshtok AM</u>. Pain at its sourse: signal transduction and propagation at the nociceptive peripheral terminals. 3rd Scientific Conference of the Institute for Medical Research Israel-Canada. <u>Winner of the Best Poster Award</u>

21. Gudes S., <u>Binshtok AM.</u> Tumor Necrosis Factor alfa rapidly modulates gating properties of tetrodotoxin-resistant sodium channels, leading to acute nociceptive hyperexcitability. SFN 2014. Washington DC.

- 22. Revah O., Tchumachenko T., Wolf F., <u>Binshtok AM.</u>, Gutnick M. Dynamic characteristics of synaptic noise in neurons of the barrel cortex are layer-specific, SFN 2014, Washington DC
- 23. Katz B, Goldstein R., Barkai O., Minke B., Bachelet I., <u>Binshtok AM</u>. Nanorobotots in the pain battlefield: programmable DNA devices for detection and blockade of hyperexcitable states of the pain pathway. Annual National Network of Excellence in Neuroscience Meeting. 2014, Netanya, Israel
- 24. Tzour A., Lev S., Yaari Y., <u>Binshtok AM</u>. Neuronal K_V7/M channels as targets for glia-neuron interactions underlying inflammation-induced CNS hyperexcitability. IBRO Meeting, 2015, Rio de Janeiro, Brazil, *Winner of the Second Best Poster Award of the IBRO meeting*
- 25. Revah O., <u>Binshtok AM.</u>, Woolf F., Neef A., Gutnick MJ. Slow asynchronous synaptic noise broadens the dynamic range of spiny stellate neurons in layer 4 of the mouse barrel cortex. SFN 2016, San Diego, USA
- 26. Barkai O., Goldstein R., Lev S., Binshtok AM. A new spice to the inflammatory soup: PDGF activates peripheral pain neurons by inhibiting Kv7/M-type potassium channels. 26nd ISFN Meeting, Eilat Israel, 2017. *Winner of the Best Poster Award*
- 27. Goldstein R., Katz B., Lev S., <u>Binshtok AM</u>. Pain at its Source: Signal Transduction and Propagation at the Nociceptive Peripheral Terminals. 2018 Annual Meeting of the Israeli Society of Physiology and Pharmacology, Tel Aviv University
- 28. Barkai O., Goldstein R., Lev S., <u>Binshtok AM</u>. A new spice to the inflammatory soup: PDGF activates peripheral pain neurons by inhibiting Kv7/M-type potassium channels. 2018 Annual Meeting of the Israeli Society of Physiology and Pharmacology, Tel Aviv University. <u>Winner of the Best Poster Award</u>
- 29. Goldstein R., Katz B., Lev S., <u>Binshtok AM</u>. Pain at its Source: Signal Transduction and Propagation at the Nociceptive Peripheral Terminals. 2018 World Congress on Pain, <u>Winner of the Best Poster Award</u>

8. Patents

- 1. <u>Binshtok AM</u>, Bean BP, Woolf CJ. Methods and compositions for modulating signal transduction and metabolism pathways. US Patent Application, 61/051,180, filed May 7, 2008
- 2. <u>Binshtok AM</u>, Method Composition and Kits for Treating Pain and Itch, Application No. 62/694,159, filed July 5, 2018

Scientific Biography

1. General Background and Graduate Work (Topic: Intrinsic and synaptic properties of layer 4 spiny stellate cells). My interest in mechanisms of pain began during my BSc studies in Physical Therapy at Ben Gurion University, where I graduated, Summa cum Laude, in 1995. Over the next 10 years, my clinical physiotherapy practice grew ever more focused on treating patients with pain, while my academic interest in pain mechanisms became a central driving force in my professional development. With time I realized that, although most patients recover well after acute trauma, those that develop chronic inflammatory or neuropathic pain usually do not respond well to currently available treatments. This realization set the stage for my decision to acquire the knowledge, training and professional

groundwork essential to investigate the fundamental mechanisms of different forms of pain within the framework of basic science.

My graduate work, under Prof. Michael Gutnick, focused on cellular and molecular characteristics of neurons composing the rodent primary somatosensory "barrel" cortex, and their synaptic connectivity. The results of my work were published in leading journals in the field (*Neuron* and *Journal of Neuroscience*; #1, #2) and my thesis was awarded *The Schlomiuk Prize* for excellence.

2. Postdoctoral Fellowship and Junior Faculty Position at Harvard Medical School (Topic: Pain-Selective Anesthesia). Continuing my focus on pain, I accepted a post-doctoral fellowship with world-renowned pain neurobiologist Prof. Clifford Woolf at Massachusetts General Hospital and Harvard Medical School. My research yielded significant gains in the understanding of pain and has contributed to advances into the development of novel and efficient techniques to diminish pain. My colleagues and I discovered a novel approach to selectively block painrelated neurons without the undesired side effects of numbness or motor paralysis that are produced by conventional local anesthetic agents. We developed a nociceptor-specific drug delivery system that exploited activated TRPV1 channels, the nociceptor-specific noxious thermo-sensitive transducer, to target charged (and therefore membrane impermeant) drug molecules selectively into pain-sensing neurons. We found that the pore of activated TRPV1 channels is large enough to pass QX-314, a charged derivative of lidocaine that is ineffective from the outside, but blocks sodium channels (and therefore excitability) from the inside of cells. Thus, activation of TRPV1 channels, paired with co-application of otherwise clinically ineffective QX-314, produces selective inhibition of pain-related signals, while sparing motoric or sensory modalities. This novel approach shows clinical promise as a long lasting regional analgesic that will preserve normal motor and sensory functions, and has been adopted by peers in academia and pharmaceutical industry worldwide. The results of this study were published in Nature (#5) and highlighted in an accompanying Editorial. This article was rated by Faculty of 1000 Medicine as "Exceptional: A landmark paper representing the top 1% of publications", and was the second highest ranked research article of all time in all categories of medicine. In addition, this publication was rated as "Exceptional" in "Faculty of 1000 Biology" receiving an all-time top 25 ranking. Subsequently, as a postdoctoral fellow and as Instructor of Anesthesia at Harvard Medical School, I continued exploring molecular mechanisms underlying pain, and published my key findings in the Journal of Neuroscience (#7) and Anesthesiology (#6, #8).

While at Harvard, I developed several successful collaborations combining my expertise in electrophysiology, imaging and behavior studies with the expertise of my colleagues in genetics, biochemistry, histology and molecular biology to help solve complex problems in pain research. The results of these collaborations were described in research articles in *Nature Medicine (#3)* and *Nature Cell Biology (#4)*. I have continued to engage this high-yield collaborative approach at The Hebrew University by fostering a collaborative attitude in my own lab.

- **3.** *PI at The Hebrew University.* As a PI in the Department of Medical Neurobiology at The Hebrew University-Hadassah School of Medicine, and as a member of the Edmond and Lily Safra Center for Brain Sciences, I have put together a multidisciplinary research group trained and equipped with cutting edge technologies. Together we aim to analyze how neurons at different levels detect, encode and transmit pain related information in normal and pathological conditions. I have outlined below the main ongoing research projects in my lab:
 - Detection of noxious information directly by nociceptive nerve terminals (Robert Goldstein, PhD student, Supported by ERC Grant). We study the mechanisms of detection and coding of noxious stimuli by nociceptive terminals, trying to identify functional molecular networks for detection of noxious stimuli in the physiologically relevant settings. We started with setting up the *in vitro* system in which we can directly activate nociceptive terminal-like processes and optically record their activity using ultrahigh-speed (up to 2000 Hz) calcium and sodium imaging. Using this cutting edge approach we found that the nociceptive terminal-like process is composed of two compartments by virtue of their dependence of functional sodium channels. The results of this work were recently published in Journal of Biomedical Optics (#21). These finding, albeit important, might not necessarily reflect the activity of nociceptive terminals in physiological conditions. Therefore, we decided to study the physiology of nociceptive terminals in vivo. Excitingly, after several years of setting up the system we were able, for the first time, to optically record the noxious stimuli evoked activity of nociceptive terminals in vivo in mouse cornea. The results of these recordings suggest the exact locations of transduction, transition and spike initiation zones in nociceptive terminals in physiological conditions. Next we are planning to use the *in vivo* model to pharmacologically dissect the identity of the ion channels which participate in the initiation and propagation of the action potential at this location. Furthermore, we will use this model to study the elements responsible for setting the excitability

of the terminals and how these settings are modulated under inflammatory conditions. We hope to check these future findings in terminals innervating the skin as well.

- Coding of pain and itch by peripheral neurons (Sagi Gudes, PhD student, Felix Blasl, postdoc, Supported by ERC Grant). We recently discovered the mechanism by which pain and itch is encoded by peripheral neurons. Using combined electrophysiology recordings and ion imaging performed by my PhD student Sagi Gudes and my postdoc Felix Blasl, together with the behavioural experiments conducted in Prof. Woolf's laboratory, we demonstrated that that although pain and itch stimuli are detected by similar transduced channels TRPV1 and TRPA1, these channels are expressed by functionally distinct pain and itch neurons thus the encoding of pain and itch is achieved already at the level of the peripheral fibers. The results of this work were published in 2013 in Nature Neuroscience (#13) and were highlighted in an Editorial. Both Prof. Woolf and I are corresponding authors for this paper.
- The role of mitochondria in controlling pain detection by nociceptive neurons (Yaki Caspi, PhD student, Supported by DIP and ERC Grants). We recently discovered that the activity of main pain- and itch-detecting TRPV1 channel is controlled by mitochondria. Using advanced mitochondrial imaging together with electrophysiological techniques we, I collaboration with Prof. Sekler, from Ben Gurion University, show that ion signaling which initiated by active TRPV1 is communicated to mitochondria via the mitochondrial calcium uniporter and sodium/calcium exchanger and that this communication controls nociception. These findings were published in BBA Molecular Cell Research in 2016 (#18).
- Mechanisms of inflammation-mediated hyperexcitability (Sagi Gudes, PhD student; Arik Tzour PhD student; Supported by ERC and DIP Grants). We are studying how different proinflammatory mediators affect the excitable properties of neurons thus leading to inflammation-mediated hyperexcitability. Using electrophysiological recording and computational modeling of Na⁺ channel gating, we have discovered that the pro-inflammatory cytokine TNFα, which is released during inflammation, rapidly increases the excitability of peripheral pain neurons, facilitating abnormal action potential firing therefore leading to inflammatory pain. This work has already yielded interesting and clinically relevant insights and has been published in Journal of Neurophysiology in 2015 (#14). Moreover, using multi-photon based calcium imaging in conjunction with electrophysiological recordings from neurons in slices, we found that inflammation causes astrocytic activation which in turn leads to blockade (via purinergic and glutamatergic metabotropic receptors) of neuronal M-current in this inflammation-induced neuronal hyperexcitability. Our manuscript describing these findings were published in Journal of Physiology in 2016 (#17).
- The effect of platelet-derived growth factor (PDGF) on the excitability of nociceptors (Omer Barkai, PhD student). We recently discovered that the Platelet-Derived Growth Factor (PDGF), which is released from epithelial cells during the inflammation, acts via PDGFR-β receptor to block M-current. Our data demonstrate that this effect of PDGFR directly excites nociceptive primary neurons leading to inflammation-induced hyperexcitability of these neurons, thus playing a prominent role in development of inflammatory pain. We are now preparing the manuscript describing these findings. Moreover, we found that M-current in primary nociceptive neurons act as a "natural voltage clamp" mechanism to prevent ectopic firing. These results were recently published in Frontiers of Molecular Neuroscience (#20).
- Mapping of neuronal projections in normal conditions (Shlomo Tsuriel, postdoc Sagi Gudes, PhD student, Supported by ERC Grant) and after nerve injury (Hodaya Leibovich, PhD student and Shlomo Tsuriel, postdoc, Supported by ERC Grant). We study how information detected by nociceptive neurons is propagated into CNS. To that end, in collaboration with Prof. Lichtman we have developed a novel multispectral labelling technique to parse projections of many neurons simultaneously. This technique entails injection, in overlapping regions of an innervated organ, with three or more different colored retrograde tracers. These tracers undergo vesicular uptake by nerve terminals and retrogradely transport to the neuronal soma. Based on the combinations and intensities of the colors in the individual vesicles transported to the cell soma, we calculate the projection sites of the neuron's axon. This neuronal positioning system (NPS) enables mapping of many axons in a simple automated way. The article describing usage of this technique in peripheral and central nervous system is recently published in Nature Methods. Prof. Lichtman and I are the corresponding authors of this paper, my postdoc Shlomo Tsuriel is a first author and my student Sagi Gudes is a second author. Currently, we are using NPS to follow nociceptive information from the periphery to the spinal cord and trigeminal nucleus. Moreover, we have modified NPS to study nerve injury related peripheral plasticity. Using this new technique, we named PAINBOW, we show that nerve-injury lead to changes in the innervation pattern of the target organs, such that the dennervated areas become reinnervated mostly by nonnociceptive neurons. This injury-mediated peripheral plasticity may underlie neuropathy-induced increases in pain. We are now finalizing the manuscript for submission.

• Characterizing pain stimuli-evoked activation of local central neuronal circuits in normal conditions and in models of chronic pain (Sagi Gudes, PhD student, Supported by ERC Grant). We are utilizing the whisker barrel system to follow the propagation of painful stimuli from the periphery and to monitor stimulus-evoked activation of local central neuronal circuits in normal conditions and in models of chronic pain. This system, with its well-defined correlation between peripheral mechanoreceptors and their central representations, is an ideal model to study stimulus-evoked synaptic plasticity. Using this system and applying focal noxious stimuli to a single whisker follicle, we identify central neurons acutely activated by these stimuli. To this end we are using intrinsic imaging-guided in vivo electrophysiological recordings and multiphoton imaging of layer 2-3 and layer 4 neurons following focal noxious stimulation. We will then test the effect of noxious stimuli on the responses of individual neurons or network activity in the barrel cortex. To this end, using virus-based delivery of the genetically encoded calcium indicator GCaMP6 to pain-related cortical neurons we are planning to perform in vivo two-photon calcium imaging in response to acute or chronic application of noxious stimuli to a single whisker follicle.

- Design and fabrication of logic-guided DNA-based nanorobots for controlled and programmable blockade of pain (Robert Goldstein, PhD student and Dr. Ben Katz, postdoc, Supported by DIP Grant). Using DNA-origami technology, we are building devices which carry modulators of neuronal activity and are controlled by an aptamer-based gate, which requires one or more biological, chemical or physical cues as its cognate keys. Thus, the modulators they carry could be released in a programmable, logically-controlled fashion. In particular, we are designing aptamer keys which target nanorobots to release their cargo in response to specific modes of pathological neuronal activity associated with pain, and, therefore, to modulate only the pathological activity while sparing normal functions. To be able to successively execute this seemingly "science fiction" and "beyond cutting edge" project I have setup an international collaborative consortium which has brought together experts in DNA-origami, biochemistry and neuroscience. This collaborative project, where I together with my collaborator from Germany Dr. Zimmermann serve as PIs, recently received funding from the prestigious DIP foundation.
- Platform for selective ablation of cancer cells via TRP-channel-mediated targeting (Hagit Raizel, PhD student, Supported by the Marie Curie Reintegration Grant and Rosetrees foundation). In this study we are using the approach I have developed in my postdoc to selectively block pain neurons to affect cancer cells. Here, we show that cytotoxic agents such as doxorubicin can be delivered into liver cancer cells in vitro through the pore of activated TRP channels expressed differentially on these cells. We are now finalizing our manuscript describing these findings ahead of submission. Meanwhile, we are building on these findings to uncover evidence of clinical relevance in vivo. Likewise, we are broadening the scope of our platform to include other types of cancer cells that express large pore ion channels that may be suitable for targeted delivery of chemotherapeutic agents.

In addition to my research activities I serve on the editorial board of PloS ONE as an Academic Editor, and as a reviewer for *eLife*, *Journal of Neuroscience*, *Anesthesiology*, *Pain*, *Molecular Pain*, *Journal of Neurophysiology*, *EMBO Molecular Medicine and others*. Since my last appointment, I was invited to lecture in more than 60 international and local conferences, as well as at universities worldwide.

I am currently involved in multiple projects, some of which received funds from the prestigious ERC and DIP foundations. I remain confident that the route I have charted will yield novel insights into fundamental aspects of pain while advancing the development of selective and effective treatment platforms.