### **BIOGRAPHICAL SKETCH**

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NAME: Shenhav Shemer

eRA COMMONS USER NAME: SHENHAVCOHEN

POSITION TITLE: Associate Professor

### **EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Bar-Ilan University, Israel	B.A.	1995	Biology
Bar-Ilan University, Israel	Ph.D.	2002	Muscle biology
Harvard Medical School, Boston, USA	Postdoc	2013	Biochemistry and muscle biology

#### A. Personal Statement

My laboratory focuses on understanding the biochemical and molecular basis of protein degradation during muscle atrophy in aging or disease (e.g. diabetes, cancer). We are specifically interested in the roles of certain key factors that trigger proteolysis in this process because their inhibition could be of major therapeutic promise. My laboratory masters two areas in biology, the biochemistry of the ubiquitin-proteasome system and muscle biology/physiology. Through the development of new methodologies, we initiated distinct lines of investigation to clarify gene effects in atrophying muscles of adult mouse. We proposed the first models for myofibril destruction during atrophy - a process that has long been uncertain. We have also identified the sequence of events promoting desmin filaments loss, which leads to the inevitable loss of myofibrils during atrophy. I expect our future work and discoveries to have broad impacts by providing foundational understanding of diverse types of wasting, highlighting how cells retain and adapt their size to the changing physiological environment. Our long-term goal is to identify rational therapies to combat wasting and promote health, improve quality of life, and increase life span of the affected individuals.

## **B.** Positions and Honors

<u>Appointments</u>	
2000-2001	Lecturer, Biotechnology engineering, Ariel University
2000-2001	Lecturer, Virology, Bar-Ilan University
2002-2006	Senior research associate and Team leader, Proteologics LtD
2011-2012	Teaching Assistant, Anatomy for Cell Biologists-dissection lab, Harvard Medical School
2011-2013	Research Fellow in Cell Biology, Harvard University
Sep 2013-2019	Assistant professor, Technion institute of Technology
2013-2014	Head, Genetic engineering lab, Technion
2014-	Lecturer, Metabolism and human Disease, Technion
2014-	Lecturer, Human physiology, Technion
Oct 2019-	Associate professor, Technion institute of Technology
2020-2022	Visiting Scholar, Harvard John A. Paulson School of Engineering and Applied Sciences
2022-	Associate of the Harvard John A. Paulson School of Engineering and Applied Sciences
2022-	Vice dean for graduate studies, Faculty of Biology, Technion

### Other Professional activity

2024-	Member, committee for research awards, Technion
2020-	Editorial board member, BBA-MCR journal

2018- 2017 2017	Member, The Israel Society for Biochemistry and Molecular Biology Invited ambassador, The American Society for Cell Biology Editorial board member, MOST Israel-Italy collaboration grant committee
2017-	Member, Scientific review and student selection committee, ISEF
2016-2017	Member, European Association for the Study of Diabetes
2013-2014	Host editor in "Frontiers in Physiology"
2013-	Israel representative at COST Actions TD1104, BM1307
2013-	Member, The American Society for Cell Biology
2013-	Member, American Physiology Society
2013-	Adhoc reviewer for German Israeli Foundation for Scientific Research and Development (GIF), Israel Science Foundation (ISF), National Science Foundation (NSF), Mars Pitsburg foundation, Michigan-Israel partnership.
2013-	Adhoc reviewer for Science, Journal of Experimental Medicine (JEM), Nature Communications, Nature Cell Biology, FASEB J, Cancer Research, Frontiers in Physiology Cell Physiology, AJP, SCWD.

#### Honors and awards

2024	Technion-wide Best Teacher Award with Distinction
2023	Levengrat award for muscle atrophy research
2023	Hitman award for muscle atrophy research
2020	Cooper Award for Excellence in Research
2020	Norman and Helen Asher Research Award
2020	ICA research award for outstanding researcher
2015	Dr. Bernard and Bobbie Lublin Cancer Research award
2014	Malat family award
2014	Robin award for biomedical research
2006-2011	Postdoctoral fellowship from Harvard University
2007-2011	Edmond J. Safra Fellowship, New York, USA
1995-2000	PhD fellowship from Bar Ilan University, Israel
1995	BA, Graduation with honors from Bar Ilan University, Israel

# C. Peer-reviewed Publications

- 1. Zbidat S, Volodin A, Fried IA, Armani A., Gilda JE, and Cohen S. Insulin receptor turnover in fasting is dependent on NAGLU-mediated β-dystroglycan deglycosylation. *BioRxiv*.
- 2. Gilda J, Nahar S, Kasiviswanathan D, Tropp N, Gilinski T, Lahav T, Mandel-Gutfreund Y, Park S and Cohen S. Proteasome gene expression is controlled by the coordinated functions of multiple transcription factor. *BioRxiv*.
- 3. Aweida D and Cohen S. The AAA-ATPase ATAD1 and its partners promote degradation of desmin intermediate filaments in muscle. *EMBO rep.* 23(12):e55175. 2022.
- 4. Gilda JE and Cohen S. Molecular mechanisms of skeletal muscle wasting in cancer. Invited book chapter. *Springer Nature*. eBook ISBN 978-3-031-09518-4. 2022.
- 5. Gilda J.E., Ko J.H., Elfassy A., TroppN., Parnis A., Ayalon B., Jhe W. and Cohen S. A semi-Automated Measurement of Muscle Fiber Size using Imaris Software. Invited. *AJP-Cell Physiology*. 321(3):C615. 2021.
- 6. Agnetti G., Herrmann H. and Cohen S. New roles for desmin in the maintenance of muscle homeostasis. Invited review. *FEBS J.* 289(10):2755. 2021.
- 7. Aweida D. and Cohen S. Breakdown of Filamentous Myofibrils by the UPS–Step by Step. Invited review. *Biomolecules*.11(1):110. 2021.
- 8. Cohen S. Role of calpains in promoting desmin depolymerization and muscle wasting. *BBA-Molecular Cell Research*. 1867(10):118788. 2020.
- 9. Goldbraikh D, Neufeld D, Eid-Mutlak Y, Lasry I, Gilda J.E, Parnis A and <u>Cohen S</u>. USP1 deubiquitinates Akt to inhibit PI3K-Akt-FoxO signaling in muscle atrophy during prolonged starvation. *EMBO Rep*. 21(4):e48791. 2020.

- 10. Eid-Mutlak Y, Aweida D, Volodin A, Dahan N, Parnis A and <u>Cohen S</u>. A signaling hub of plakoglobin, insulin receptors and dystrophin glycoprotein complex regulates muscle size. *Nature Communications*. 11(1):1381. 2020.
- 11. Yatsenko AS, Kucherenko MM, Xie Y, Aweida D, Urlaub H, Scheibe RJ, <u>Cohen S</u>, Shcherbata HR. Profiling of the muscle-specific dystroglycan interactome reveals the role of Hippo signaling in muscular dystrophy and age-dependent muscle atrophy. *BMC Medicine*. 18(1):8. 2020.
- 12. Aweida D, Rudesky I, Volodin A, Shimko E & Cohen S. GSK3-β promotes calpain-1-mediated desmin filament depolymerization and myofibril loss in atrophy. *J Cell Biology*. 217(10):3698-3714. 2018
- 13. Shiloh R, Gilad Y, Ber Y, Eisenstein M, Aweida D, Bialik S, <u>Cohen S</u> & Kimchi A. Non-canonical activation of DAPK2 by AMPK constitutes a new pathway linking metabolic stress to autophagy. *Nature Communications*. 9(1):1759. 2018.
- 14. Bassat, E., Mutlak, YE., Yifa, O., Genzelinakh, A., Shadrin, IY., Baruch-Umansky, K., Yifa, O., Kain, D., Rajchman, D., leach, J., Riabov Bassat, D., Udi, Y., Sarig, R., Sagi, I., Martin, JF., Bursac, N., Cohen, S., and Tzahor, E. The extracellular matrix protein agrin promotes heart regeneration in mice. *Nature*. 547(7662):179-184. 2017.
- 15. Volodin, A., Kosti, I., Goldberg, A.L. and Cohen, S. Myofibril breakdown during atrophy is a delayed response requiring the transcription factor PAX4 and Desmin Depolymerization. *PNAS*. 114(8):E1375-E1384. 2017.
- Commentary: Losing pieces without disintegrating: Contractile protein loss during muscle atrophy. PNAS. 114(8):1753-1755.
- 16. Piterman R, Braunstein I, Isakov E, Ziv T, Navon A, Cohen S, Stanhill A. VWA domain of S5a restricts the ability to bind ubiquitin and Ubl to the 26S proteasome. *Mol Biol Cell*. 25(25):3988-98. 2014.
- 17. Cohen S, Lee D, Zhai B, Gygi SP, Goldberg AL. Trim32 reduces Pl3K-Akt-FoxO signaling in muscle atrophy by promoting plakoglobin-Pl3K dissociation. *J Cell Biol.* 204(5):747-58. 2014.
- 18. Cohen S, Zhai B, Gygi SP, Goldberg AL. Ubiquitylation by Trim32 causes coupled loss of desmin, Z-bands, and thin filaments in muscle atrophy. *J Cell Biol*. 198(4):575-89. 2012.
- 19. Cohen S, Brault JJ, Gygi SP, Glass DJ, Valenzuela DM, Gartner C, Latres E, Goldberg AL. During muscle atrophy, thick, but not thin, filament components are degraded by MuRF1-dependent ubiquitylation. *J Cell Biol.* 185(6):1083-95. 2009.
- Leslie, M. Muscle atrophy through thick but not thin. J Cell Biol 185(6): 931, 2009.
- Selected as highlighted article on J Cell Biol cover.
- Selected for the spotlight on research by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).
- 20. Cohen S, Dovrat S, Sarid R, Huberman E, Salzberg S. JAK-STAT signaling involved in phorbol 12-myristate 13-acetate- and dimethyl sulfoxide-induced 2'-5' oligoadenylate synthetase expression in human HL-60 leukemia cells. *Leuk Res.* 29(8):923-31. 2005.
- 21. Alroy I, Tuvia S, Greener T, Gordon D, Barr HM, Taglicht D, Mandil-Levin R, Ben-Avraham D, Konforty D, Nir A, Levius O, Bicoviski V, Dori M, Cohen S, Yaar L, Erez O, Propheta-Meiran O, Koskas M, Caspi-Bachar E, Alchanati I, Sela-Brown A, Moskowitz H, Tessmer U, Schubert U, Reiss Y. The trans-Golgi network-associated human ubiquitin-protein ligase POSH is essential for HIV type 1 production. *PNAS*. 102(5):1478-83. 2005.
- 22. Salzberg S, Vilchik S, Cohen S, Heller A, Kronfeld-Kinar, Y. Expression of a PKR dominant-negative mutant in myogenic cells interferes with the myogenic process. *Exp Cell Res.* 254:45-54. 2000.

# D. Research Support

2023-2028	HORIZON-HLTH-2022-DISEASE-06-04-two-stage, DREAMS consortium
2023-2024	NEVET
2022-2023	EuroTech alliance grant
2021-2023	Duchenne UK
2020-2023	Israel Ministry of Health
2020-2022	Israel Cancer Association, grant for a distinguished researcher
2020-2022	Norman and Helen Asher Space grant
2019-2024	Israel Science Foundation
2015-2018	Israel Science Foundation equipment grant

2015-2018	Israel Science Foundation
2015-2018	Ministry of Science, Technology and Space
2014-2017	Niedersachsen - Israel Cooperation
E. Invited talks	
2009	Guest speaker, Beth Israel Deaconess. Boston, MA, USA.
2009	Muscle in health and disease meeting, Society of General Physiologists. Woods Hole,
2000	MA, USA.
2009	The ubiquitin family meeting. Cold Spring Harbor Laboratory, NY, USA.
2010	Biology of ubiquitin and the ubiquitin-like systems meeting. HUJI, Israel.
2011	Muscle mass regulation meeting. Lecce, Italy.
2011	Molecular mechanisms of muscle growth and wasting in health and disease meeting.
	Centro Stefano Franscini, Ascona, Switzerland.
2011	The ubiquitin family meeting, CSHL, NY, USA.
2012	The ubiquitin meeting. HUJI, Israel.
2014	13th International Congress on Neuromuscular Diseases meeting. Nice, France.
2014	Muscle meeting. Florida, USA.
2015	Guest speaker, Max Planck Institute for Biophysical Chemistry. Goettingen, Germany.
2015	The annual meeting of the physiology society. Cardiff, UK.
2016	The 2016 International Wingate Congress of Exercise and Sport Sciences meeting.
0040	Wingate, Israel.
2016	Annual Broad Institute-ISF Cell Circuits Symposium. Broad Institute, MA, USA.
2016	Molecules in living cell and innovative medicine, X Jakub K. Parnas Conference, Joint
	Conference of Polish Biochemical Society, Ukrainian Biochemical Society and Israeli
2016	Society of Biochemistry and Molecular Biology. Wroclaw, Poland.
2016	Skeletal and Cardiac Myogenesis Workshop. Weizmann Institute, Israel.
2016	7th Proteasome and autophagy congress. Clermont-Ferrand, France.
2017 2017	Zavalkoff International Symposium. McGill University, Canada.
2017	ZOMES IX conference. Rome, Italy.
2017	Guest speaker, Rockefeller University. NYC, USA.
2017	The ubiquitin family meeting. CSHL, NY, USA.  Myogenesis, Gordon research conference. Lucca, Italy.
2018	8th proteasome and autophagy congress. Clermont-Ferrand, France.
2019	Guest speaker, Harvard Medical School. Boston, USA.
2020	Protein Homeostasis in Health & Disease meeting, CSHL, NY, USA. Virtual meeting.
2020	CEB 2020, Boston, USA. Virtual meeting.
2022	Gordon Research Conference. Vermont, USA
2022	FASEB Calpain Meeting. May 2022. Palais du Pharo, Marseille, France
2022	Minerva workshop on Metabolism and Aging, Herzliya, Israel.
2022	Guest speaker, Centre of Research in Myology, INSERM, France.
2023	European Meeting on Intermediate Filaments. Noordwijkerhout, The Netherlands.
2023	Keynote speaker. Victorian Muscle Network Symposium, University of Melbourne,
	Australia.
2024	Russian National Conference on Muscle and Evercise Physiology, Moscow

Russian National Conference on Muscle and Exercise Physiology, Moscow.