BIOGRAPHICAL SKETCH

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NAME: Nahmias, Yaakov

eRA COMMONS USER NAME: YNAHMIAS

POSITION TITLE: Professor, Chair Department of Bioengineering, Director of the Alexander Grass Center for Bioengineering.

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Technion, Israel Institute of Technology, Haifa, Israel	B.Sc.	09/1999	Chemical Engineering *(Summa cum laude)*
University of Minnesota, Minneapolis, MN	Ph.D.	08/2004	Biomedical Engineering
Harvard Medical School, Massachusetts General Hospital, Boston, MA	Postdoc	08/2006	Bioengineering

A. Personal Statement

My work is focused on the applications of tissue engineering and microfluidics for the study of metabolic programming: understanding how cells process information to make metabolic decisions. My early work established the first microscale 3D printing of living vascular tissues[1], and outlined the metabolic requirements of primary hepatocytes[2]. The NIH-funded work established the culture technology for HuREL, the first human-on-chip company on the market, and the first groundbreaking liver decellularization[3]. In 2009, I moved to the Hebrew University of Jerusalem establishing a large European Research Council (ERC) funded laboratory focused on developing tools to study central carbon metabolism in pluripotent stem cells and human hepatocytes. We demonstrated that glycolysis induced hyper-acetylation of pluripotent stem cells, which is rapidly lost upon differneitation[4], and that microbial-derived secondary bile acids activated PXR-dependent CYP450 enzymes in fetal hepatocytes immediately after birth[5]. More recently, we developed a genetic switch that allowed us to expand human liver cells without losing metabolic function[6], a cell library commercialized by Upcyte Technologies. Finally, our microfluidic liver-on-chip technology currently enables us to precisely monitor changes in central carbon metabolism in real-time[7]. We used this approached to explain the idiopathic toxicity of acetaminophen (Tylenol) and the idiosyncratic toxicity of troglitazone (Rezulin), in work that was heralded as major technological innovation by the European H2020 program, and commercialized by Tissue Dynamics.

1. **Y. Nahmias**, D. J. Odde, Micropatterning of living cells by laser-guided direct writing: application to fabrication of hepatic-endothelial sinusoid-like structures, *Nature Protocols, 1(5):2288-2296(2006)*
2. S. Kidambi, R. Yarmush, E. Novik, P.B. Chao, M.L. Yarmush, **Y. Nahmias,** Oxygen-mediated enhancement of metabolism, functional polarization, gene expression, and drug clearance in co-cultures of primary hepatocytes, *PNAS* 106(37):15714-9 (2009)
3. B. Uygun, A. Soto-Gutierrez, H. Yagi, M.L. Izamis, M.A. Guzzardi, C. Shulman, J. Milwid, N. Kobayashi, A. Tilles, F. Berthiaume, M. Hertl, **Y. Nahmias**, M.L. Yarmush, K. Uygun. Organ reengineering through development of a transplantable recellularized liver graft using decellularized liver matrix. *Nature Medicine. 16(7):814-20. (2010)*
4. A. Moussaieff, M. Rouleau, D. Kitsberg, M. Cohen, D. Barasch, A. Nemirovski, S.S. Shen-Orr, I. Laevsky, M. Amit, D. Bomze, B. Elena-Herrmann, T. Scherf, M. Nissim-Rafinia, S. Kempa, J. Itskovitz-Eldor E. Meshorer, D. Aberdam, **Y. Nahmias**. Glycolysis-mediated changes in acetyl-CoA and histone acetylation control the early differentiation of embryonic stem cells. *Cell Metabolism 21(3): 392-402. (2015)*
5. Y. Avior, G. Levy, M. Zimerman D. Kitsberg, R. Schwartz, R. Sadeh, A. Moussaieff, M. Cohen, J. Itskovitz-Eldor, **Y. Nahmias.** Microbial-Derived Lithocholic Acid and Vitamin K2 Drive the Metabolic Maturation of Pluripotent Stem Cells Derived Hepatocytes. *Hepatology 2(1): 265-78. (2015)*
6. G. Levy, D. Bomze, S. Heinz, S.D. Ramachandran, A. Noerenberg, M. Cohen, O. Shibolet, E. Sklan, J. Braspenning, **Y. Nahmias**. Long-term culture and expansion of primary human hepatocytes. *Nature Biotechnology 33(12): 1264-1271. (2015)*

7. D. Bavli, S. Prill, E. Ezra, G. Levy, M. Cohen, M. Vinken, J. Vanfleteren, M. Jaeger, **Y. Nahmias**, Real-time monitoring of metabolic function in liver-on-chip microdevices tracks the dynamics of mitochondrial dysfunction. *PNAS 113(16):E2231-40. (2016)*

B. Positions and Honors

Positions and Employment

2004-2006	Shriners Fellow, Shriners Burns Hospital, Boston, MA
2006-2009	Instructor, Center for Engineering in Medicine, Harvard Medical School, Boston, MA
2009-2013	Assistant Professor, Department of Bioengineering, Hebrew University of Jerusalem, Israel
2012-	Chair, Department of Bioengineering, Hebrew University of Jerusalem, Israel
2014-2015	Adjunct Professor, Department of Chemical Engineering, Northeastern University, Boston, MA
2015-2016	Visiting Professor, Broad Institute of MIT and Harvard, Cambridge, MA
2013-	Associate Professor, Department of Bioengineering, Hebrew University of Jerusalem, Israel

Industry Positions

2009-2010	Consultant, HμREL Corporation
2015-	Consultant, L'Oréal Research & Innovation
2016-	Founder, Chief Scientific Advisor, SuperMeat
2016-	Founder, Chief Scientific Officer, Tissue Dynamics

Other Experience and Professional Memberships

2011-	ERC Review Committee: Applied Life Sciences and Biotechnology
2012-	Editorial Board, Organogenesis
2012-2014	Scientific Board, SignGene, German-Israeli Helmholtz Graduate School
2014-2015	Chair, Committee on Alternative Models, Israel Ministry of Health
2016	Track Chair, Nano and Micro Technologies, BMES Annual Meeting
2016-	Scientific Board, Hebrew University Entrepreneurship Center
2016-	Editorial Board, Annual Review of Biomedical Engineering
2009-	Member, American Institute of Chemical Engineering (AICHE)
2009-	Member, Biomedical Engineering Society (BMES)
2006-	Member, American Association for the Study of the Liver (AASLD)

Honors and Awards *(selected)*

2004	BMEI Director Award, Medical Alley
2003	Director Award, Design of Medical Devices
2004	Shriners Fellow, Shriners Hospitals
2008	NIH, Research Scientist Career Development Award (K01)
2009	Young Investigator Award, Cell Transplant Society
2010	Faculty Fellow, Golda Meir Foundation
2010	European Research Council (ERC) Starting Grant
2011	Marie Curie Fellow, International Reintegration Award
2014	Rappaport Prize for Biomedical Sciences
2016	European Research Council (ERC) Consolidator Grant

C. Contributions to Science

1. I completed my undergrad at the Technion, *Summa Cum Laude*, where I worked with Prof. Mizrahi on solid-form insulin microencapsulation, and became an inventor on a patent (WO2008132727) that was licensed by Novartis. Then during my postdoctoral work, I identified a small molecule, naringenin, derived from grapefruit, capable of blocking HCV production through a PPAR-dependent mechanism. I created a nanocomplex that increased naringenin bioavailability, allowing to us run a successful clinical trial at Massachusetts General Hospital. My focus on nanotechnology also led to the development of self-assembled KGF-based therapies for ulcers and together with the late Prof. Folkman the revolutionary new anti-cancer drug *Lodamin*, hailed as “mother lode of tumor angiogenesis”.

a. **Y. Nahmias**, J. Goldwasser, M. Casali, D. van Poll, T. Wakita, R. T. Chung, M. L. Yarmush, ApoB dependent HCV Secretion is Inhibited by the Grapefruit Flavonoid Naringenin, *Hepatology 47(5):1437-45 (2008)*
b. O. Benny, O. Fainaru, A. Adini, F. Cassiola, L. Bazinet, I. Adini, E. Pravda, **Y. Nahmias**, S. Koirala, G. Corfas, R. J. D'Amato, J. Folkman, An orally delivered small-molecule formulation with antiangiogenic and anticancer activity, *Nature Biotechnology. 26(7):799-807 (2008)*
c. P. Koria, H. Yagi, Y. Kitagawa, Z. Megeed, **Y. Nahmias**, R. Sheridan, M.L. Yarmush, Self-assembling elastin-like peptides growth factor chimeric nanoparticles for the treatment of chronic wounds. *PNAS. 108(3):1034-9 (2011)*
d. M. Shulman, M. Cohen, A. Soto-Gutierrez, H. Yagi, H. Wang, J. Goldwasser, C.W. Lee-Parsons, O. Benny-Ratsaby, M.L. Yarmush, **Y. Nahmias**, Enhancement of Naringenin Bioavailability by Complexation with Hydroxypropoyl-β-cyclodextrin, *PLoS One. 6(4):e18033 (2011).*

2. Throughout my career I had a strong interest in liver tissue engineering as I aimed to create functional models of the liver to study metabolic processes, disease progression and regeneration. My work established the first 3D printing of complex liver sinusoids with single cell resolution, inspiring countless other 3D printing works. I demonstrated HGF-dependent migration of hepatocytes to endothelial cells forming micro-organs that maintained function for over a month *in vitro*. In parallel, I took an active part in the first liver decellularization, a method that retains the complete vascular tree of solid organs for tissue engineering. My work then established the role of endothelial cells in induced basal surface polarization of hepatocytes and their role in enhancing HCV infection. The same culture technique recently allowed us to study the metabolic determinants of HCV infection, showing PPAR/FXR dependent metabolic anti-viral response. This was the first demonstration that host cells can resist viruses metabolically, suggesting new avenues for therapy. To expand our tools we re-engineered regeneration by releasing primary human hepatocytes from cell-cycle arrest using low level E6/E7 expression. We built a library of cells and showed the first patient-to-patient variation to HCV infection and drug toxicity. This work was heralded as one of the most exciting breakthroughs of Israeli science in 2015, and commercialized by Upcyte® Technologies.

a. **Y. Nahmias**, D. J. Odde, Micropatterning of living cells by laser-guided direct writing: application to fabrication of hepatic-endothelial sinusoid-like structures, *Nature Protocols, 1(5):2288-2296(2006)*
b. **Y. Nahmias**, R. Schwartz, W-S. Hu, C. Verfaillie, and D. J. Odde, Endothelium-mediated hepatocyte recruitment in the establishment of liver-like tissue *in vitro*, *Tissue Engineering 2006;12(6):1627-1638*
c. B. Uygun, A. Soto-Gutierrez, H. Yagi, M.L. Izamis, M.A. Guzzardi, C. Shulman, J. Milwid, N. Kobayashi, A. Tilles, F. Berthiaume, M. Hertl, **Y. Nahmias**, M.L. Yarmush, K. Uygun. Organ reengineering through development of a transplantable recellularized liver graft using decellularized liver matrix. *Nature Medicine. 16(7):814-20. (2010)*
d. G. Levy, M.A. Guzzardi, N. Habib, D. Kitsberg, D. Bomze, B.E. Uygun, K. Uygun, M. Trippler, J.F. Schlaak, O. Shibolet, E.H. Sklan, M. Cohen, J. Timm, N. Friedman, **Y. Nahmias**, Nuclear Receptors Control Pro- and Anti-Viral Metabolic Response to HCV Infection. *Nature Chemical Biology 12, 1037–1045 (2016)*
e. G. Levy, D. Bomze, S. Heinz, S.D. Ramachandran, A. Noerenberg, M. Cohen, O. Shibolet, E. Sklan, J. Braspenning, **Y. Nahmias**. Long-term culture and expansion of primary human hepatocytes. *Nature Biotechnology 33(12): 1264-1271. (2015)*

3. My interests in nanotechnology and liver tissue engineering intersected early in my career when I co-edited a book with Prof. Bhatia titled "Microdevices in Biology and Medicine". There I took an active part in the development of the living cell array, and a technique to maintain human hepatocyte function using high oxygen co-cultures. The latter patent (US20120129207) became the core technology for HμREL, the first human-on-chip company on the market aiming to replace animal experiments in drug development. More recently I developed a liver-on-chip microdevice capable of tracking the dynamics of central carbon metabolism in *real time* using integrated nanoparticles. The technique allowed us to identify a CYP450-independent mechanism of acetaminophen (Tylenol®) that may underlie its idiopathic kidney toxicity. Recently, we also identified a CYP450 independent sub-threshold toxicity of troglitazone (Rezulin®) that may underlie its idiosyncratic toxicity. The work was featured in Cell Systems, F1000 Medicine, heralded as major innovation by Europe H2020, and commercialized by Tissue Dynamics.

a. Microdevices in Biology and Medicine (Methods in Bioengineering Series), **Y. Nahmias**, S.N. Bhatia, Editors, Artech House, Aug (2009)
b. S. Kidambi, R. Yarmush, E. Novik, P.B. Chao, M.L. Yarmush, **Y. Nahmias,** Oxygen-mediated enhancement of metabolism, functional polarization, gene expression, and drug clearance in co-cultures of primary hepatocytes, *PNAS* 106(37):15714-9 (2009)
c. T. J. Maguire, E. Novik, P. Chao , J. Barminko, **Y. Nahmias**, M. L. Yarmush, K. C. Cheng, Design and application of microfluidic systems for in vitro pharmacokinetic evaluation of drug candidates. Curr Drug Metab. 10(10):1192-9. (2009)
d. S. Prill, D. Bavli, G. Levy, E. Ezra, E. Schmälzlin, M.S. Jaeger, M. Schwarz, C. Duschl, M. Cohen, **Y. Nahmias**. Real-time monitoring of oxygen uptake in hepatic bioreactor shows CYP450-independent mitochondrial toxicity of acetaminophen and amiodarone. *Arch Toxicol. 90(5):1181-91. (2016)*
e. D. Bavli, S. Prill, E. Ezra, G. Levy, M. Cohen, M. Vinken, J. Vanfleteren, M. Jaeger, **Y. Nahmias**, Real-time monitoring of metabolic function in liver-on-chip microdevices tracks the dynamics of mitochondrial dysfunction. *PNAS 113(16):E2231-40. (2016)*

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Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1V5UHyTLOHhQD/bibliography/51589558/public/?sort=date&direction=ascending.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

06BX14SFYN Nahmias (PI) 02/01/15-01/31/17
Generation of induced pluripotent stem cells (iPSC) derived Hepatic Progenitor Cells (HPC) for wide scale engraftment using micro-fluidics. This is a bi-national grant with Stuart Forbes aiming to differentiae la population of liver stem cells for the treatment of cirrhosis.
Role: PI

ISF 31349 Nahmias (PI) 10/01/14-09/30/17
In vitro maturation of embryonic stem cell derived liver organoid
This project aims to study the last stage of fetal liver maturation using hiPS cells.
Role: PI

BSF 2013002 Nahmias (PI) 10/01/14-09/30/18
Cleavable Surface Coatings for Microfluidic Devices Applications
This is a bi-national grant with Shashi Murthy aiming to use microfluidics to isolate stem cells from liver and skin tissues for cell engraftment.
Role: PI

ERC 681870 Nahmias (PI) 09/01/16-08/31/21
Tracking the Dynamics of Human Metabolism using Spectroscopy-Integrated Liver-on-Chip Microdevices
This consolidator grant aims to create physiological rhythms in microfluidic devices and use spectroscopy to measure changes in intracellular metabolism.
Role: PI

Completed Research Support

33BX12HGYN Nahmias (PI) 03/01/13-06/30/16
Elucidating the role of microvascular branching in liver morphogenesis
This was a bi-national BIRAX grant with Holger Gerhardt aiming to study the interactions between endothelial cells and hepatocytes during regeneration in a microfluidic device.
Role: PI

FP7 266777 Verfaillie (PI) 01/01/11-12/21/16
Hepatic Microfluidic Bioreactor (HeMiBio)
This was a consortium grant co-funded by the European Commission and Cosmetics Europe aiming to create a liver-on-chip microdevice using pluripotent stem cells derived hepatocytes.
Role: Co-PI

ERC 242699 Nahmias (PI) 04/01/10-03/31/15
Microfabrication-Based Rational Design of Transcriptional-Metabolic Intervention for the Treatment of HCV Infection. This starting grant aimed to elucidate the metabolic determinates of HCV infection in primary hepatocyte co-cultures using microfluidic control.
Role: PI

IRG 248417 Nahmias (PI) 01/01/11-02/28/14
Gene network-based maturation of embryonic stem cell-derived hepatocytes in a microfabricated array
This Marie Curie award aimed to study the nuclear receptor network involved in stem-cell derived hepatocyte maturation using a library of GFP-reporters.
Role: PI

MOS-Japan 9645 Nahmias (PI) 01/01/10-11/30/13
Organ Engineering: Development of Artificial Liver Tissue Using Embryonic Stem Cells
This was a bi-national grant with Yukou Kitagawa aiming to develop porcine decellularized liver matrix and repopulate it with stem cell derived hepatocytes.
Role: PI

NIH R01EB009327 Murthy (PI) 05/01/10-04/30/2015
Microfluidic Cell Separation for Tissue Engineering and Regenerative Medicine
This work aimed to use microfluidics to isolate stem cells from tissue using micro-post arrays
Role: Co-Investigator

NIH K01DK080241 Nahmias (PI) 03/01/08-07/31/2013
Gene Network Based Differentiation of Stem Cells in a Microfabricated Array
This was an NIH research scientist career award, where David Scadden and Mehmet Toner mentored me. The project aimed to study stem cell differentiation in microfluidic array using GFP-reporters.
Role: PI

Licensed Patents

1. E. Shimoni, O. Ramon, I. Kopelman, S. Mizrahi, N. Salzman, **Y. Nahmias**, A. Oren. Oral Delivery of Proteins and Peptides, (WO 2008/132,727), November 11, 2008
1. **Y. Nahmias**, RT. Chung, ML. Yarmush, Naringenin Complexes and Methods of Use Thereof, (WO 2010/042,633), April 15, 2010
2. **Y. Nahmias**, E. Novik, ML. Yarmush, R. Freedman, Compositions and Methods of Functionally Enhanced In Vitro Cell Culture System, (WO 2010/062,911), June 3, 2010
3. E. Fried, Y. Hayut, D. Planar, **Y. Nahmias**, Guided endotracheal intubation system, (WO 2014/184,796), May 16, 2013
4. **Y. Nahmias**, P. Sebastian, J. Magnus, B. Danny, S. Elmar, Method and system for continuous monitoring of toxicity (EP 2015/160,661), Mar 24, 2014
5. T. Hasin, Y. Goldstein, A. Buxboim, **Y. Nahmias**, Jugular venous pressure assessment, (US 62/182,584), 21 June 2015
6. R. Weiss, A. Shochat, C. Vinitzky, Y. Lacher, A. Buxboim, **Y. Nahmias**, Detection of peripheral arterial disease, (US 62/182,587), 21 June 2015
7. **Y. Nahmias**, G. Levy, A. Noerenberg, S. Heinz, J. Braspenning, Genetic Induction of Metabolically Functional, Polarized Cultures of Proliferating Human Hepatocytes, (US Patent 62/200,212), August 3, 2015
8. **Y. Nahmias**, Systems and methods for growing edible meat in vitro, (US Patent 62/360,495), July 11, 2016