BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Podbilewicz, Benjamin	Full Professor of Biology
eRA COMMONS USER NAME (credential, e.g., agency login) PBENJAMIN	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Instituto Politecnico Nacional, Mexico City, Mexico	B.Sc.	08/86	Chemistry, Bacteriology and Parasitology
Yale University, New Haven, USA	Ph.D.	12/91	Cell Biology
MRC Laboratory of Molecular Biology, Cambridge, UK	Postdoc	01/96	Developmental Genetics

A. Personal Statement

We are using the nematode *Caenorhabditis elegans* to investigate cell fusion, organ formation, and nerve cell development. The wealth of anatomical, genetic, developmental, and molecular information available for *C. elegans* provides a multidisciplinary and powerful approach for these studies. Our work has focused on the study of one fundamental biological question: **How do cells fuse?** Cells fuse during fertilization and formation of organs. For example, macrophages, eye lens cells, placental cells, and muscle human cells fuse. We also work on how cells migrate, change shapes, and sculpt organs and how cell fusion and organ formation evolve. I pioneered research on cell fusion in *C. elegans* in 1990 when I proposed, while I was in my last year of graduate school at Yale Cell Biology, to characterize programmed cell fusion in *C. elegans*. A year later I started to work on this fundamental question in the lab of John White at the MRC-Laboratory of Molecular Biology, Cambridge UK. I described the pathways of embryonic and postembryonic cell-cell fusions in the epidermis and vulva of the worm and initiated genetic screens and molecular studies of candidate fusogens. In my lab at the Technion-Israel Institute of Technology we initially approached cell fusion by mutational analysis, obtaining many mutations in two genes that we found are critical for the cell fusion process. We identified EFF-1 and AFF-1, two type I membrane proteins essential and sufficient for developmental cell fusion in *C. elegans*. EFF-1 and AFF-1 are the founders of the first family of eukaryotic cell fusion proteins (fusogens). EFF-1 and AFF-1 from nematodes can fuse heterologous insect cells. EFF-1 is required in both fusing cells and the process is via the universal intermediate of hemifusion. We purified and determined the three-dimensional structure of EFF-1 protein, we are testing its fusogenic activities in cells and in reconstituted in vitro systems. Our ultimate goal is to understand the molecular and physicochemical mechanisms of cell membrane fusion. We have accomplished a complete description of the cellular events leading to the formation of an organ. Using genetic analyses we identify genes that function to control different cell fusion events in *C. elegans* and in other organisms and how this process is regulated in development. We now focus on fertilization, the development of vulva, epidermis, muscles and pharynx.

Neuronal arborization. We discovered that EFF-1 is also required to sculpt complex neuronal trees (arbors) required for sensing strong mechanical stimuli (pain receptors). We found that EFF-1 trims abnormal neuronal branches as a novel quality control mechanism. EFF-1 works in specific neurons (PVDs and FLPs) by fusing and retracting branches. Thus, we identified that a genuine fusogen can restrict branching by dendrite retraction and auto-fusion. We have identified additional genes that participate in the generation and maintenance of complex neuronal trees and we hope that our discoveries in *C. elegans* may help to understand and repair degenerative diseases of the nervous system and accidental breaking of neurons.

Evolution of organogenesis. We study cellular events during morphogenesis of the vulva across species. We found that changes in the direction of cell divisions can result in differences in size and shape of the vulva. We found that evolution of most vulval characters are biased and proposed that evolution of the vulva in nematodes is governed by selection and/or selection-independent constraints and not by stochastic processes. We are also trying to find missing fusogens that act in fertilization and muscle formation in worms and mammals. My goal is to understand how cell-cell fusion and organ development evolve.

B. Positions and Honors

Positions and Employment

1991-1996	Posdoctoral Fellow. MRC-Laboratory of Molecular Biology, Cambridge, England. (Advisor: John White)
1994-1996	Scientific Staff. MRC-Laboratory of Molecular Biology, Cambridge, England.
1996-1999	Lecturer. Department of Biology, Technion-Israel Institute of Technology, Israel.
1997-present	Director. Confocal Laser-Scanning Microscopy Research Unit, Technion, Israel.
1999-2003	Senior Lecturer. Department of Biology, Technion-IIT, Israel.
2003-2005	Visiting Scientist. Laboratory of Cellular and Molecular Biophysics, NICHD, NIH.
2003-2008	Associate Professor. Department of Biology, Technion-IIT, Israel.
2005-2008	Elected representative of the department of biology in the Technion Senate, Israel.
2006-present	Director of the microscopy unit, Technion-IIT, Israel.
2006-present	Life Sciences steering committee, Technion-IIT, Israel.
2007-2009	Head of recruitment, Biology and Lockey Center for Life Sciences and Engineering.
2008-present	Full Professor. Department of Biology, Technion-IIT, Israel.
2010-2012	Committee for Academic Prizes, Technion-IIT, Israel.

Other Experience and Professional Memberships

Ad hoc reviewer for the following journals:

Biochimica et Biophysica Acta, *Biological Chemistry*, *Biology of the Cell, Cell*, *Current Biology*, *Development*, *Developmental Biology*, *Developmental Cell*, *DNA Repair*, *FEBS Journal, Gene Expression Patterns, Genes and Function*, *Genetics*, *Journal of Biological Chemistry*, *Journal of Cellular Physiology*, *Nature, Nature Methods, Nature Reviews Molecular Cell Biology*, *PLoS Biology*, *Science*, *Proceedings of the National Academy of Sciences, USA, Trends in Cell Biology*

Ad hoc reviewer for the following granting agencies:

Israel Science Foundation (ISF), US-Israel Binational Science Foundation (BSF), German-Israeli Foundation for Scientific Research & Development (GIF), Research Grants Council (Hong Kong), Association Francaise contre les Myopathies (AFM) France, Israel Science Foundation Study Section member (2007). Human Frontier Science Program (HFSP).

2012-present	**Editorial Board, *F1000 Research***
2011-present	**Editorial Board, *Worm***
2006-present	**Contributor to Faculty of 1000 Biology**
2006-present	**Editorial Board, Developmental Dynamics**

Referee of academic tenure and promotions at the following institutions:

Albert Einstein College of Medicine, Cornell University, Fred Hutchinson Cancer Research Center, The Pennsylvania State University, University of North Carolina at Chapel Hill, University of Connecticut, National Institutes of Health (NIH), USA, Yale University, Harvard University

Professional Memberships:

American Society for Cell Biology, Genetic Society of America, Israeli Society for Developmental Biology, Israeli Society for Biochemistry and Molecular Biology, Israel Society for Microscopy

Awards and Honors

1989	Distinguished Alumnus (diploma), IPN, Mexico
2000-2003	The Israel Science Foundation Award from the Charles H. Robson Fund for Basic Research in the Life Sciences, Israel
2005	The Henry Taub Prize for Excellence in Research, Israel
2008	The Teva Research Grant, Israel
2012	Bingzhi Forum Professorship, Institute of Zoology, Chinese Academy of Sciences, Beijing.
2012	Grass Fellow, Radcliffe Institute for Advanced Study, Harvard University, USA.

Recent Invited Talks (2009-2014)

Gordon Research Conference on Cell-Cell Fusion. New Hampshire, USA, Vice-Chair. June 2009
Workshop on *Live Microscopy* at The International Meeting on *C. elegans*, Los Angeles, USA. June 2009
Lipid Dynamics 49th Annual Meeting of the ASCB, San Diego, USA. Co-Chair and talk. December 2009
C. elegans development and Gene Expression, Heidelberg, Germany (Invited Keynote Speaker). June 2010
European *C. elegans* Neurobiology Meeting. Crete, Greece. October 2010
Conference on Bioscience and Society: Organisms as Living Systems**.** Ljubljana, Slovenia. October 2010
The Johns Hopkins University. Department of Molecular Biology & Genetics Seminar. USA. November 2010
National Institutes of Health. NICHD. Bethesda, USA. November 2010
Developmental Biology. National Center for Biological Sciences. Bangalore, India. January 2011
Nobel Symposium. Protein Chemistry - Applications to Combat Diseases. Copenhagen. Denmark. 2011
National Meeting of Biochemistry. Mexican Society for Biochemistry. Oaxaca, Mexico. (Plenary Talk). 2012
Keystone Symposium on Membranes in Motion: From Molecules to Disease. Tahoe City. (Invited Talk). 2012
Radcliffe Institute for Advanced Study, Harvard University, Cambridge, USA. (Fellow presentation). 2012
National Institutes of Health, NICHD, Bethesda, USA. (Invited talk). 2013
Yale University. Department of Cell Biology, New Haven, USA. (Invited talk). June 2013
CNRS, Gif-Sur-Yvette, France. (Invited talk). December 2013
SignGene International Differentiation Cancer Workshop. Haifa, Israel. (Invited talk). January 2014

Participation in Organizing Conferences

The 2008 Congress of the Federation of the Israel Societies for Experimental Biology (ILANIT). Eilat, Israel.
Gordon Research Conference (GRC) on Cell-Cell Fusion. USA. 2009. Elected Vice-Chair.
From Darwin to Evo-Devo, A Symposium in honor of the 150th anniversary of Darwin's Origin of Species. Haifa, Israel. 2009. Organizing Committee.
Gordon Research Conference (GRC) on Cell-Cell Fusion. USA. 2011. Chair.
The International Meeting on *C. elegans*, Los Angeles, USA. June 2011. Organizing Committee.
Congress of the International Society for Developmental Biology. México. June 2013. International Committee.
6th Israel Live Imaging Forum Symposium, Haifa, Israel. Organizing Committee. 2012
EMBO-Katzir Workshop on Cell-Cell Fusion. Ein Gedi, Israel. Organizing Committee. 2013
The 2014 Congress of the Federation of the Israel Societies for Experimental Biology (ILANIT). Eilat, Israel.
20th International *C. elegans* meeting. UCLA, USA. Co-chair. 2015

C. Selected Peer-reviewed Publications (Selected from 45 publications)

Most relevant to the current application

1. **Podbilewicz, B.,** and White, J.G. (1994). Cell fusions in the developing epithelia of *C. elegans. Dev. Biol.* **161**:408-424.
2. Mohler, W.A., Shemer, G., del Campo, J., Valansi, C., Opoku-Serebuoh, E., Scranton, V., Assaf, N., White, J.G., and **Podbilewicz, B.** (2002). The type I membrane protein EFF-1 is essential for developmental cell fusion. *Dev. Cell*. **2**:355-362.
3. **Podbilewicz, B.,** Leikina, E., Sapir, A., Valansi, C., Suissa, M. Shemer, G. and Chernomordik, L.V. (2006) The *C. elegans* developmental fusogen EFF-1 mediates homotypic fusion in heterologous cells and in vivo. *Dev. Cell.* **11**:471-481.
4. Sapir, A., Choi, J., Leikina, E., Avinoam, O., Valansi, C., Chernomordik, L.V., Newman, A.P., and **Podbilewicz, B.** (2007) AFF-1, a FOS-1-Regulated Fusogen, Mediates Fusion of the Anchor Cell in *C. elegans*. *Dev. Cell.* **12**:683-698.
5. Kiontke, K., Barrière, A., Kolotuev, I., **Podbilewicz, B**., Sommer, R., Fitch, D. and Felix, M.-A. (2007). Evolution of development in the nematode vulva system: trends, stasis and drift. *Curr. Biol.* **17**:1925-1937.
6. Oren-Suissa, M., Hall, D., Treinin, M., Shemer, G., and **Podbilewicz, B.** (2010). The Fusogen EFF-1 Controls Sculpting of Mechanosensory Dendrites. *Science* **328**:1285-1288.
7. Avinoam, O., Fridman, K., Valansi, C., Abutbul, I., Zeev-Ben-Mordehai, T., Maurer, U.E., Sapir, A., Danino, D., Gruenewald, K., White, J.M., and **Podbilewicz, B.** (2011). Conserved Eukaryotic Fusogens Can Fuse Viral Envelopes to Cells. Science **332**, 589-592.
8. Perez-Vargas, J., Krey, T., Valansi, C., Avinoam, O., Haouz, A., Jamin, M., Raveh-Barak, H., **Podbilewicz, B.*** and Rey, F.A.* (2014). Structural basis of eukaryotic cell-cell fusion *Cell*. **157**, 407-419.

Additional publications of importance to the field (in chronological order)

1. Podbilewicz, B., and Mellman, I. (1990). ATP and cytosol requirements for transferrin recycling in intact and disrupted MDCK cells. *EMBO J.* **9**: 3477-3487.
2. Sharma-Kishore, R., White, J.G., Southgate E. and Podbilewicz, B. (1999). Formation of the vulva in *Caenorhabditis elegans*: A paradigm for organogenesis. *Development*. **126**: 691-699.
3. Shemer, G. and Podbilewicz, B. (2002). LIN-39/Hox Triggers Cell Division and Represses EFF-1/Fusogen-Dependent Vulval Cell Fusion. *Genes & Dev*. **16**: 3136-3141.
4. Shemer, G., Suissa, M., Kolotuev, I., Nguyen, K. C. Q., Hall, D. H. and Podbilewicz, B. (2004). EFF-1 is sufficient to initiate and execute tissue-specific cell fusion in *C. elegans*. *Curr Biol* **14**, 1587-1591.
5. Cassata, G., Shemer, G., Morandi, P., Donhauser, R., Podbilewicz, B., and Baumeister, R. (2005) *ceh-16/engrailed* patterns the embryonic epidermis of *Caenorhabditis elegans*. *Development.* **132**:739-749.
6. Gattegno, T., Mittal, A., Valansi, C., Nguyen, K.C.Q., Hall, D.H., Chernomordik, L.V. and Podbilewicz, B. (2007) Genetic control of fusion pore expansion in the epidermis of *Caenorhabditis elegans*. *Mol. Biol. Cell.* **18**:1153-1166.
7. Kiontke, K., Barrière, A., Kolotuev, I., Podbilewicz, B., Sommer, R., Fitch, D. and Felix, M.-A. (2007) Evolution of development in the nematode vulva system: trends, stasis and drift. *Curr. Biol.* **17**:1925-1937.
8. Margalit, A., Neufeld, E., Feinstein, N., Wilson, K.L., Podbilewicz, B. and Gruenbaum, Y. (2007) Barrier-to-autointegration factor (BAF) blocks premature cell fusion regulates vulva formation, cell migration and germ cell development and survival, and maintains adult muscle integrity in *C. elegans*. *J. Cell. Biol*. **178**:661-673.
9. Chen, A., Leikina, E., Melikov, K., Podbilewicz, B., Kozlov, M. and Chernomordik, C.V. (2008) Fusion-pore expansion during syncytium formation is restricted by an actin network. *J Cell Sci.* **121**:3619-28.
10. Oren-Suissa, M., and Podbilewicz, B. (2010). Evolution of programmed cell fusion: Common mechanisms and distinct functions. *Developmental Dynamics* **239**:1515-1528.
11. Avinoam, O. and **Podbilewicz, B**. (2011). Eukaryotic Cell-Cell Fusion Families. *Curr Top Membr* **68**: 209-234. Chernomordik, L. V. and Kozlov, M. (Eds). Elsevier.
12. Aguilar, P.S., Baylies, M.K., Fleissner, A., Helming, L., Inoue, N., **Podbilewicz, B.**, Wang, H., and Wong, M. (2013). Genetic basis of cell-cell fusion mechanisms. *Trends Genet*. **29**:427-437.
13. **Podbilewicz, B**. Virus and Cell Fusion Mechanisms. (2014). *Ann Rev of Cell and Dev Biol.* **30:**In Press
14. Greenblum, A., Sznitman, R., Fua, P., Arratia, P.E., Oren, M., **Podbilewicz, B.**, and Sznitman, J. (2014). Dendritic tree extraction from noisy maximum intensity projection images in *C. elegans*. Biomedical engineering online **13**:74.

D. Research Support

Ongoing Research Support

European Research Council Advanced Grant (ERC) Podbilewicz (PI) 2011-2016
Mechanisms of Cell Fusion in Eukaryotes

The Israel Science Foundation (ISF). Podbilewicz (PI) 2012-2017
Mechanisms of dendrite auto-fusion and retraction during arborization.

Completed Research Support *(2007-2012)*

R13 HD061041-01 Mohler (PI) 2009
2009 Cell-Cell Fusion Gordon Research Conference. Role: Vice-Chair

The Israel Science Foundation (ISF) Podbilewicz (PI) 2004-2008
Regulation of the cell fusion machinery in *C. elegans*.

German Israeli Foundation (GIF) Podbilewicz and Bossinger (PIs) 2007-2010
Disassembly Mechanism of Junctional Complexes in Epithelia of *C. elegans*

F.I.R.S.T, Israel Science Foundation (ISF) Podbilewicz (PI) 2007-2010
Searching for the mammalian muscle cell fusogenic factors using *C. elegans* as a test tube

The Israel Science Foundation (ISF). Podbilewicz (PI) 2008-2012
Deciphering the molecular basis of sperm-egg fusion.