

CV & Publications

Prof. Ben- Zion Levi

Academic degrees

B.Sc. (1977)	Tel Aviv University, Dept. of Biology
M.Sc. (1979)	Tel Aviv University, Dept. of Microbiology, Faculty of Life Sciences
D.Sc. (1984)	Technion- Israel Institute of Technology, Dept. of Food Eng. and Biotechnology

At Technion since 1989

Academic appointments

1977 – 1979	Instructor, Department of Microbiology. Tel Aviv University, Israel
1979 – 1984	Research Assistant, Department of Food Engineering and Biotechnology, Technion Haifa, Israel
1985 – 1986	Visiting Fellow, Laboratory of Developmental and Molecular Immunity, NICHD, NIH
1986 – 1989	Visiting Associate, Laboratory of Developmental and Molecular Immunity, NICHD, NIH
1989 – 1997	Senior Lecturer, Dept. of Food Engineering and biotechnology, Technion, Haifa 32000, Israel
1997 – 2003	Associate Professor, Dept. of Food Engineering and biotechnology, Technion, Haifa 32000, Israel
2003	Professor, Dept. of Biotechnology and Food Engineering, Technion, Haifa 32000, Israel
2004	The Lily and Silvan Marcus Chair in Life Sciences

Research Interests

Mammalian gene regulation; Transcriptional modulation of the immune system; Role of Interferon Regulatory factors (IRFs) in myelopoiesis and myeloleukemias; The role of IRFs in conferring resistance to pathogens

Publications

1. **Levi, B.Z** and Ultizur, S.: Proflavin and norharman induce luciferase synthesis under anaerobiosis. Arch. Microbiol. 134:261-164, 1983.
2. Ultizur, S., Weiser, I., **Levi, B.Z.**, and Barak, M.: Determination of 100 chemicals by the improved bioluminescence test for mutagenic agents. Third International Symposium on Analytical Application Bioluminescence and Chemiluminescence. Birmingham, U.K., 1984.
3. Ben-Itzhak, J., **Levi, B.Z**, Shor, T., Lanir, A., Bassan, H.M., and Ultizur, S.: The formation of mutagenic metabolites of benzo(a)pyrene by the isolated perfused rat liver, as detected by the bioluminescence test. Mutat. Res. 147:107-112, 1985.
4. **Levi, B.Z**, Kuhn, J.C., and Ultizur, S.: The mutagenic activity of hydrazines in the bioluminescence test. Mutat. Res. 173:233-237, 1986.
5. Kaufmann, Y., Silverman, T., **Levi, B.Z**, and Ozato, K.: Induction of c-ets and c-fos gene expression upon antigenic stimulation of memory-like cytolytic hybridoma. J. Exp. Med. 166:810-815, 1987.
6. Wan, Y-J., **Levi, B.Z**, and Ozato, K.: Induction of c-fos expression by interferons and its possible role in neonatal development. J. Interferon Res. 8:105-112, 1988.
7. **Levi, B.Z**, Kasik, J.w., and Ozato, K.: c-fos antisense RNA blocks expression of c-fos gene in F9 embryonal carcinoma cells. Cell Differentiation. 25:95-102, 1988.
8. **Levi, B.Z**, and Ozato, K.: Constitutive expression of c-fos antisense RNA blocks c-fos gene induction by interferon and by phorbol ester and reduces c-myc expression in F9 embryonal carcinoma cells. Genes and Development. 2:554-566, 1988.
9. **Levi, B.Z**, Kasik, J.W., Burke, P.A., Prywes, R., Roeder, R.G., Appella, E., and Ozato, K.: Neonatal induction of a nuclear protein that binds to the c-fos enhancer. Proc. Natl. Acad. Sci. USA. 86:2262-2266, 1989.
10. Lazarovici, P., **Levi, B.Z**, Lelkes, P.I., Koizumi, S., Fujita, K., Matsuda, Y., Ozato, K., and Guroff, G.: K-252a inhibits the increase in c-fos transcription and increase in intracellular calcium produced by nerve growth factor in PC12 cells. J. Neuroscience Res. 23:1-8, 1989.

11. Massa, P.T., Cowan, E.P., **Levi, B.Z.**, Ozato, K., and McFarlin, D.E.: Inducibility of class I MHC molecules on mouse astrocytes varies in strains with different H-2 haplotypes. J. Neuroimmunology. 24:125-132,1989.
12. Rudkin, B.B., Lazarovici, P., **Levi, B.Z.**, Abe, Y., Fugita, K., Guroff, G.: Cell cycle-specific action of nerve growth factor in PC12 cells: Differentiation without proliferation. EMBO J. 8:3319-3325,1989.
13. Hamada, K., Gleason, S.L., **Levi, B.Z.**, Appella, E., and Ozato, K.: A new member of nuclear hormone receptor superfamily binds to both the regulatory element of the major histocompatibility class I genes and the estrogen response element. Proc. Natl. Acad. Sci. USA. 86:8289-8293,1989.
14. Driggers, P., A., Ennist, D., L., Gleason, S., L., Mak, W-H., Marks, M., S., **Levi, B.Z.**, Flanagan, J., R., Appella, E., Ozato, K. An Interferon-gamma regulated protein that binds the interferon inducible enhancer element of the major histocompatibility complex class I genes. Proc. Natl. Acad. Sci. USA. 87:3743-3747,1990.
15. Mizrachi, Y., Naranjo, J.R., **Levi, B.Z.**, Pollard, H.B., Lelkes, P.I. PC12 cells differentiate into chromaffin cell-like phenotype in coculture with adrenal medullary endothelial cells. Proc. Natl. Acad. Sci. USA. 87:6161-6165,1990.
16. Ono, S.J., Bazil, V., **Levi, B.Z.**, Ozato, K., Strominger, J.L. Transcription of a subset of human class II major histocompatibility complex genes is regulated by a nucleoprotein complex that contains c-fos or antigenically related protein. Proc. Natl. Acad. Sci. USA. 88:4304-4308,1991.
17. Nagata, T., Segars, J.H., **Levi, B.Z.**, Ozato, K. Retinoic acid dependent trans-activation of major histocompatibility complex class I promoters by nuclear hormone receptor H-2RIIBP in undifferentiated embryonal carcinoma cells. Proc. Natl. Acad. Sci. USA. 89:937-941,1992.
18. Flanagan, J.R., Becker, K.G., Ennist, D.L., Gleason, S.L., Driggers, P.H., **Levi, B.Z.**, Appella, E., and Ozato, K. Cloning of a negative transcription factor that binds to the upstream conserved region of Moloney murine leukemia virus. Mol. Cell. Biol. 12: 38-44, 1992.
19. Massa, P.T., Hirschfeld, S., **Levi, B.Z.**, Quigley, L.A., Ozato, K., McFarlin, D.E. Expression of major histocompatibility complex (MHC) class I genes in astrocytes correlates with the presence of nuclear factors that bind to constitutive and inducible enhancers. J Neuroimmunol. 41:35-42, 1992.
20. Marks, M.S., **Levi, B.Z.**, Segars, J.H., Driggers, P.H., Hirschfeld, S., Nagata, T., Appella, E., Ozato, K. Nuclear hormone receptor H-RIIBP expressed from a baculovirus vector binds multiple hormone response elements. Mol. Endo. 6:219-230,1992. (The first two authors made an equal contribution).\

21. Neutra, R., **Levi, B.Z**, Shoham, Y. Optimization of protein-production by the baculovirus expression system in shake flasks. Appl. Microbiol. Biotechnol. 37: 74-78, 1992.
22. Cohen, T., Gitay-Goren, H., Neufeld, G., **Levi, B.Z** High levels of biologically active vascular endothelial growth factor are produced by the baculovirus expression system. Growth Factors 7: 131-138, 1992.
23. Weisz, A., Marx, P., Sharf, R. Appella, Driggers, P.H., E. Ozato, K., **Levi, B.Z** Human interferon consensus sequence binding protein is a negative regulator of enhancer elements common to interferon-inducible genes. J. Biol. Chem. 267: 25589-25596, 1992.
24. Etkin, E., Carp, L., **Levi, B.Z** *Spodoptera frugiperda* sf-9 cells nuclear factor binds to a specific sequence on the baculovirus polyhedrin promoter. Virus Res. 31:343-356, 1994.
25. Tessler, S., Rockwell, P., Hicklin, D., Cohen, T., **Levi, B.Z**, Lemischka, I. R., Witte, L., and Neufeld, G. Heparin modulates the interaction of VEGF₁₆₅ with soluble and cell associated *flk-1* receptors J. Biol. Chem. 1269: 12456-12461, 1994.
26. Soker, S., Goldstaub, D., Svahn, C.M., Vlodavsky, I., **Levi, B.Z**, and Neufeld, G. Variations in the size and sulfation of heparin modulate the effect of heparin on the binding of VEGF(165) to its receptors. Biochem. Biophys. Res. Commun. 203:1339-1347, 1994.
27. Weisz, A., Kirchhoff, S., and **Levi, B.Z**. Interferon Consensus Sequence Binding Protein is a conditional repressor of interferon inducible promoters. International Immunology 6:1125-1131, 1994.
28. Cohen, T., Gitay-Goren, H., Sharon, R., Shibuya, M., Halaban, R., **Levi, B.Z**, & Neufeld, G. VEGF₁₂₁, a vascular endothelial growth factor (VEGF) isoform lacking heparin binding ability, requires cell-surface heparan sulfates for efficient binding to the VEGF receptors of human melanoma cells. J Biol Chem 270: 11322-11326, 1995.
29. Gengrinovitch, S., Greenberg, S. M., Cohen, T., Gitay-Goren, H., Rockwell, P., Maione, T. E., **Levi, B.Z**, and Neufeld, G. Platelet factor-4 inhibits the mitogenic activity of VEGF₁₂₁ and VEGF₁₆₅ using several concurrent mechanisms. J. Biol. Chem. 270:15059-15065, 1995.
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33. Thornton, A.M., Ogryzko, V.V., Dent, A., Sharf, R., **Levi, B.Z**, Kanno, Y., Staudt, L.M., Howard, B.H., and Ozato, K. A dominant-negative mutant of an IFN regulatory factor family protein inhibits both type-I and type-II IFN-stimulated gene-expression and antiproliferative activity of IFNs. J. Immunol. 157:5145-5154, 1996.
34. Pitcovski, J., Di-Castro, D., Shaaltiel, A., Azriel, A., Gutter, B., Yarkoni, E., Michael, A., Krispel, S., **Levi, B.Z** Insect-cell derived VP2 of infectious bursal disease virus confers protection against the disease in chickens. Avian Diseases 40:753-761, 1996.
35. Neufeld, G., Cohen, T., Gitay-Goren, H., Poltorak, Z., Tessler, S., Sharon, R., Gengrinovitch, S., & **Levi, B.Z** Similarities and differences between the vascular endothelial growth factor (VEGF) splice variants. Cancer Metastasis Rev, 15: 153-158, 1996.
36. Sharf, R., Meraro, D., Azriel, A., Thornton, A.M., Ozato, K., Petricoin, E.F., Lerner, A.C., Schaper, F., Hauser, H., **Levi, B.Z.** Phosphorylation events modulate the ability of ICSBP to interact with interferon regulatory factors and to bind DNA. J. Biol. Chem. 272:9785-9792, 1997.
37. Wolffe, A. P., J. Wong, Q. Li, **Levi, B. Z.**, Shi, Y. B. Three steps in the regulation of transcription by the thyroid hormone receptor: establishment of a repressive chromatin structure, disruption of chromatin and transcriptional activation. Biochem. Soc. Trans. 25:612-615, 1997.
38. Wong, J., Q. Li, **Levi, B. Z.**, Y. B. Shi, A. P. Wolffe. Structural and functional features of a specific nucleosome containing a recognition element for the thyroid hormone receptor. EMBO J. 16:7130-7145, 1997.
39. Akiri, G., Nahari, D., Finkelstein, Y., Le, S.Y., Elroy-Stein, O., **Levi, B.Z** Regulation of vascular endothelial growth factor (VEGF) expression is mediated by internal initiation of translation and alternative initiation of transcription. Oncogene 17: 227-236, 1998.
40. Schaper, F., Kirchoff, S., Posern, G., Koster, M., Oumard, A., Sharf, R., **Levi, B.Z.**, and Hauser, H. Functional domains of interferon regulatory factor I (IRF-1). Biochem.J. 335:147-157, 1998.

41. Pitcovski, J., Goldberg, D., **Levi, B.Z.**, Di-Castro, D., Azriel, A., Krispel, S., Maray, T., and Shaaltiel, Y. Coding region of segment A sequence of a very virulent isolate of IBDV- comparison with isolates from different countries and virulence. Avian. Dis.42:497-506, 1998.
42. Pitcovski J, **Levi B.Z.**, Maray T, Di-Castro D, Safadi A, Krispel S, Azriel A, Gutter B, Michael A: Failure of viral protein 3 of infectious bursal disease virus produced in prokaryotic and eukaryotic expression systems to protect chickens against the disease. Avian.Dis. 43:8-15, 1999.
43. Finkelstein Y, Faktor O, Elroy-Stein O, **Levi B.Z.** The use of bi-cistronic transfer vector for the baculovirus expression system. J. Biotechnol. 75:33-44, 1999.
44. Meraro, D., S. Hashmueli, B. Koren, A. Azriel, A. Oumard, S. Kirchhoff, H. Hauser, S. Nagulapalli, M.L. Atchison, and **Levi, B.Z.** Protein-protein and DNA-protein interactions affect the activity of lymphoid specific IRFs. J.Immunol. 163: 6468-6478, 1999.
45. Yehuda, H., Goldway, M., Gutter, B., Michael, A., Godfried, Y., Shaaltiel, Y., **Levi, B.Z.**, and Pitcovsky, J. Transfer of antibodies elicited by baculovirus-derived VP2 of a very virulent bursal disease virus strain to progeny of commercial breeder chickens.Avian Pathol. 29:13-19, 2000.
46. Cohen H., Azriel A., Cohen T., Meraro D., Hashmueli S., Bech-Otschir D., Kraft R., Dubiel W., and **Levi B.Z.** Interaction between ICSBP and CSN2 (Trip15) – a possible link between IRF signaling and the COP9/Signalosome. J. Biol. Chem.275:39081-39089, 2000.
47. Kirchhoff S., Oumard A., Nourbakhsh M., **Levi B.Z.**, Hauser H. Interplay between repressing and activating domains defines the transcriptional activity of IRF-1. Eur. J. Biochem. 267: 6753-6761, 2000.
48. Merediz S.A., Schmidt M., Hoppe G.J., Alfken J., Meraro D., **Levi B.Z.**, Neubauer A., Wittig B. Cloning of an interferon regulatory factor 2 isoform with different regulatory ability. Nucleic Acids Res. 28: 4219-24, 2000.
49. Meiron, M., Anunu, R., Scheinman, J.E., Hashmueli, S., and **Levi, B.Z.** New isoforms of VEGF are translated from alternative initiation CUG codons located in its 5'UTR.Biochem. Biophys. Res. Commun. 282: 1053-1060, 2001.
50. **Levi, B.Z.**, Hashmueli, S., Gleit-Kielmanowicz, M., Azriel, A., Meraro, D. ICSBP\IRF8 Transactivation – A Tale of Protein-Protein Interaction. J. Interferon & Cytokine Res.22: 153-160, 2002.
51. Meraro, D., Gleit-Kielmanowicz, M., Hauser, H., and **Levi, B.Z.** ISG15 is synergistically activated through interactions between the myelocyte/lymphocyte specific transcription factors, PU.1, IRF-8\ICSBP and IRF-4: Characterization of a new subtype of ISRE. J. Immunol. 168:6224-6231, 2002.

52. Hashmueli, S., Gleit-Kielmanowicz, M., Meraro, D., Azriel, A., Melamed, D., and **Levi, B.Z.** A truncated IRF-8\ICSBP acts as dominant negative, interferes with endogenous protein-protein interactions, and leads to apoptosis of immune cells. *Int. Immunol.* 15:807-815 2003.
53. Alter-Koltunoff, M., S. Ehrlich, N. Dror, A. Azriel, M. Eilers, H. Hauser, H. Bowen, C. H. Barton, T. Tamura, K. Ozato, and **B. Z. Levi.** 2003. Nramp1 mediated innate resistance to intraphagosomal pathogens is regulated by IRF-8, PU.1 and Miz-1. *J Biol.Chem.* 278:44025-44032.
54. Bowen, H., A. Lapham, E. Phillips, I. Yeung, M. Alter-Koltunoff, **B. Z. Levi,** V. H. Perry, D. A. Mann, and C. H. Barton. 2003. Characterization of the murine Nramp1 promoter: requirements for transactivation by Miz-1. *J Biol.Chem.* 278:36017-36026.
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57. Kanno Y, **Levi B.Z.,** Tamura T, Ozato K. Immune Cell-Specific Amplification of Interferon Signaling by the IRF-4/8-PU.1 Complex. 2005. *J. Interferon Cytokine Res.*25: 770-779.
58. Dror, N., Alter-Koltunoff, M., Azriel, A., Amariglio, N., Jacob-Hirsch, J., Zeligson, S., Morgenstern, A., Tamura, T., Hauser, H., Rechavi, G., Ozato, K., and **Levi, B. Z.**2007. Identification of IRF-8 and IRF-1 target genes in activated macrophages.*Mol.Immunol* 44:338-346.
59. Dror, N., Rave-Harel, A. Burchert, A. Azriel, T. Tamura, P. Tailor, A. Neubauer, K. Ozato, and **B. Z. Levi.** 2007. IRF-8 is indispensable for the expression of PML and the formation of nuclear bodies in myeloid cells. *J Biol.Chem.* 282:5633-5640.
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61. Alter-Koltunoff, M., S. Goren, J. Nousbeck, C. G. Feng, A. Sher, K. Ozato, A. Azriel, and **B. Z. Levi.** 2008. Innate Immunity to Intraphagosomal Pathogens Is Mediated by Interferon Regulatory Factor 8 (IRF-8) That Stimulates the Expression of Macrophage-specific Nramp1 through Antagonizing Repression by c-Myc. *J Biol.Chem.* 283:2724-2733.
62. Lee, K. Y., H. Geng, K. M. Ng, J. Yu, A. van Hasselt, Y. Cao, Y. X. Zeng, A. H. Wong, X. Wang, J. Ying, G. Srivastava, M. L. Lung, L. D. Wang, T. T. Kwok, **B. Z.**

- Levi, A. T. Chan, J. J. Sung, and Q. Tao.** 2008. Epigenetic disruption of interferon-gamma response through silencing the tumor suppressor interferon regulatory factor 8 in nasopharyngeal, esophageal and multiple other carcinomas. *Oncogene*, 27:5267–5276.
63. **Khalfin-Rabinovich Y., and B.Z. Levi.** 2010. PML, an interferon inducible gene, is a key component for myeloid cell differentiation to macrophages. *Cytokine, Special Issue (1-2) SI*: 44-46.
64. **Khalfin-Rabinovich Y., Weinstein A., and B.Z. Levi.** 2011. PML is a key component for the differentiation of myeloid progenitor cells to macrophages. *Int Immunol.* 23:287-296.