

BIOGRAPHICAL SKETCH

NOVEMBER 2003

NAME	POSITION TITLE		
Lothar Hennighausen, Ph.D.	Laboratory Chief, NIDDK, NIH		
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Marburg, Germany	BS	1977	Biology
University of Köln, Germany	Diploma	1979	Biology
University of Köln, Germany	Doctorate	1982	Genetics
Harvard Medical School	Postdoctoral	1983 - 1985	Genetics

Employment

National Institute of Diabetes and Digestive and Kidney Diseases Principal Investigator and Group Leader	1985 - 1991
Max-Planck-Institute for Biophysical Chemistry, Göttingen, Germany Visiting Scientist and Humboldt Fellow	1992 - 1993
National Institute of Diabetes and Digestive and Kidney Diseases Chief, Developmental Biology Section	1991 - 1997
Max-Planck-Institute for Biochemistry, Martinsried - München, Germany Humboldt Scholar and Visiting Professor	2002 - 2003
National Institute of Diabetes and Digestive and Kidney Diseases Senior Biomedical Research Service, National Institutes of Health Chief, Laboratory of Genetics and Physiology, Bethesda, Maryland	1997 - date

Prizes, Fellowships and Honored Lecture Invitations

- Olaf Pearson Memorial Lecture, Case Western Reserve University (2003)
- Presidential Lecture, Society for the Study of Reproduction (2002)
- Alexander-von-Humboldt Research Award (2001)
- Keynote Address, Mouse Models for Prostate Cancer, The Jackson Laboratory (2001)
- Keynote Address, American Society for Urology, Houston (2000)
- Seminars in Cell Biology, Baylor College of Medicine (2000)
- Endocrine Grand Rounds, National Institutes of Health (2000)
- Keynote Address, Molecular and Cell Biology Program, Ohio University (1999)
- Featured Speaker, IBC Conference on Production of Blood Plasma Proteins, Boston (1999)
- Seminars in Breast Cancers, Delaware Breast Cancer Coalition, Delaware Medical Association (1999)
- Seminars in Clinical Oncology, National Cancer Institute, Bethesda (1998)
- Massachusetts Breast Cancer Coalition, Boston University School of Medicine (1996)
- Keynote Address, Graduate Students Retreat, Texas A&M (1996)
- Featured Speaker, MD/P.D. Program, Baylor College of Medicine (1985)
- Fellowships from EMBO, Deutsche Forschungsgemeinschaft, and the Alexander-von-Humboldt Foundation
- Honors Program in Molecular Biology, University of Edinburgh (Scotland) (1977 - 1978)

Professional Experience and Service

- More than 300 lectures at Academic Institutions and at International Conferences
- Organizer of conferences and workshops at the NIH and the Jackson Laboratory
- Member, Mouse Model Consortium for Human Cancer
- Teaching at Harvard Medical School, Einstein College of Medicine and the Marine Biology Center at Woods Hole

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- Editorial Board (past and present) of 'Molecular Endocrinology', 'Endocrinology', 'Cell Growth and Differentiation', 'Molecular Biology Reports', 'Transgenic Research' and 'Breast Cancer Research'. Guest editor of the 'Oncogene' issue on Mouse Models for Breast Cancer
 - Review Panels at the NCI, NIDDK, the DOD Breast Cancer Initiative and the NCI of Canada
 - Developer of the "Biology of the Mammary Gland" Web site (<http://mammary.nih.gov>)
 - Developer of 'HistoBank' the Interactive Histology Atlas (<http://histology.nih.gov>)
 - Co-developer of the MicroArray Explorer (<http://www-lecb.ncifcrf.gov/mgapDB/mae>)

Dr. Hennighausen has trained more than 40 scientists. Former members from my laboratory hold or held faculty positions at the Universities of Nebraska, Missouri, Utah, UCLA, Edinburgh (Great Britain), Regensburg and Munich (Germany), Madrid (Spain), Tokushima and Osaka (Japan), Kwangju (Korea), the Scripps Institute and work in Government Research Institutes in France and Israel and for the NCI. Others have joined Biotech firms, including, GeneLogic, Human Genome Sciences, Boehringer Ingelheim and the American Red Cross. Some members joined investment and consulting firms. Former technicians are now in Medical School, Graduate School and MD/PhD programs.

Publications (33 selected out of more than 170 with a total of more than 6000 citations)

- Renou, J.-P., Bierie, B., Miyoshi, K., Cui, Y., Djiane, J., Reichenstein, M., Shani, M. and **Hennighausen, L.** (2003) Identification of genes differentially expressed in mouse mammary epithelium transformed by an activated β -catenin. *Oncogene*, 29, 4594-4610.
- Li, W., Qiao, W., Chen, L., Xu, X., Dang, X., Li, D., Li, C., Brodie, S.G., Meguid, M.M., **Hennighausen, L.** and Deng, C.X. (2003) Squamous cell carcinoma and mammary abscess formation through squamous metaplasia in Smad4/Dpc4 conditional knockout mice. *Development*, in press.
- Long, W., Wagner, K.U., Lloyd, K.C.K., Binart, N., Shillingford, J.M., **Hennighausen, L.** and Jones, F. (2003) Conditional deletion of ErbB4 in the mammary gland identifies ErbB4 as an obligate mediator of Stat5 activation and epithelial functional differentiation. *Development*, 130, 5257-5268.
- Wagner, K.U., Krempler, A., Qi, Y., Park, K., Henry, M.D., Triplett, A.A., Riedlinger, G., Rucker, E.B. and **Hennighausen, L.** (2003) TSG101 is essential for cell growth, proliferation, and cell survival of embryonic and adult tissue, *Mol. Cell. Biol.*, 23, 150-163.
- Miyoshi, K., Meyer, B., Gruss, P., Cui, Y., Renou, J.-P., Morgan, F.V., Smith, G.H., Reichenstein, M., Shani, M., **Hennighausen, L.** and Robinson, G.W. (2002) Mammary epithelial cells are not able to execute prolactin receptor-Stat5 signals in the absence of the helix-loop-helix inhibitor Id2. *Mol. Endo.*, 16, 2892-2901.
- Zhao, L., Melenhorst, J. and **Hennighausen, L.** (2002) IL6 activates Stat3 in mammary epithelium and its loss results in delayed mammary gland involution. *Mol. Endo.*, 16, 2902-2912.
- Humphreys, R., Bierie, B., Zhao, L., Raz, R., Levy, D. and **Hennighausen, L.** (2002) Deletion of Stat3 blocks mammary gland involution and extends functional competence of the secretory epithelium in the absence of lactogenic stimuli. *Endocrinology*, 143, 3641-3650.
- Shillingford, J.M., Miyoshi, K., Robinson, G.W., Grimm, S.L., Rosen, J.M., Neubauer, H., Pfeffer, K. and **Hennighausen, L.** (2002) Jak2 is an essential tyrosine kinase involved in pregnancy-mediated development of mammary secretory epithelium. *Mol. Endo.* 16, 563-570.
- Miyoshi, K., Shillingford, J.M., Le Provost, F., Gounari, F., Bronson, R., von Boehmer, H., Taketo, M.M., Cardiff, R.D., Khazaie, K. and **Hennighausen, L.** (2002) Activation of β -catenin signaling in differentiated mammary secretory epithelium induces transdifferentiation into epidermis. *Proc. Natl. Acad. Sci. U.S.A.*, 99, 219-224.
- Miyoshi, K., Shillingford, J.M., Smith, G.H., Grimm, S.L., Wagner, K.U., Oka, T., Rosen, J.M., Robinson, G.W. and **Hennighausen, L.** (2001) Signal transducer and activator of transcription 5 (Stat5) controls the specification and proliferation of mammary alveolar epithelium, *J. Cell Biol.*, 155, 531-542.
- **Hennighausen, L.** and Robinson, G.W. (2001) Signaling pathways in the mammary gland. *Developmental Cell*, 1, 467-475.
- Walton, K.D., Wagner, K.-U., Rucker, E.B., Shillingford, J.M., Miyoshi, K. and **Hennighausen, L.** (2001) Conditional deletion of the bcl-x gene from mouse mammary epithelium results in accelerated apoptosis during involution but does not compromise cell function during lactation. *Mech. of Development*, 109, 281-293.

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- Gallego, M. I., Binart, N., Robinson, G.W., Okagaki, R., Coschigano, K., Perry, J., Kopchick, J., Oka, T., Kelly, P.A. and **Hennighausen, L.** (2001) Prolactin, growth hormone and epidermal growth factor activate Stat5 in different cell types of the mammary gland and exert overlapping but distinct developmental effects. *Developmental Biology*, 229, 163-175.
 - Wagner K-U., Estefania C., Rucker, E., Riedlinger, G, Broussard, C., Schwartzberg, P.L., Siebenlist, U., **Hennighausen, L.** (2000) Conditional deletion of the bcl-x gene from erythroid cells results in hemolytic anemia and profound splenomegaly. *Development*, 127, 4949-4958.
 - Rucker, E., Dierisseau, P., Wagner, K.-U., Garrett, L., Wynshaw-Boris, A., Flaws, J. and **Hennighausen, L.**, (2000). Bcl-x and Bax regulate mouse primordial germ cell survival and apoptosis during embryogenesis. *Mol. Endo.* 7, 1038-1052.
 - Xu, X., Wagner, K.-U., Larson, D., Weaver, Z., Li, C., Ried, T., **Hennighausen, L.**, Wynshaw-Boris, A. and Deng, C. (1999). Conditional knock-out of Brca1 in mammary epithelial cells results in blunted ductal morphogenesis and tumor formation. *Nature Genetics*, 10, 37-43.
 - **Hennighausen, L.** and Robinson, G.W. (1998) Think globally, act locally: the making of a mouse mammary gland. *Genes and Development* 12, 449-455.
 - Liu, X., Gallego, M.I., Smith, G.H., Robinson, G.W. and **Hennighausen, L.** (1998) Functional rescue of Stat5a-null mammary tissue through the activation of compensating signals including Stat5b. *Cell Growth & Diff.* 9, 795-803.
 - Robinson, G.W., Johnson, P.F., **Hennighausen, L.** and Sterneck, E.(1998) The C/EBP β transcription factor regulates epithelial cell proliferation and differentiation in the mammary gland. *Genes and Development* 12, 1907-1916.
 - Wagner, K.-U., Wall, R.J., St-Onge, L., Gruss, P., Garrett, L., Wynshaw-Boris, A., Li, M., Furth, P.A. and **Hennighausen, L.** (1997) Cre mediated gene deletion in the mammary gland. *Nucleic Acids. Res.* 25, 4323-4330.
 - Robinson, G.W. and **Hennighausen, L.** (1997) Inhibins and activins regulate mammary epithelial cell differentiation through mesenchymal-epithelial interactions. *Development* 124, 2701-2708.
 - Liu, X., Robinson, G.W., Wagner, K.-U., Garrett, L., Wynshaw-Boris, A. and **Hennighausen, L.** (1997) Stat5a is mandatory for adult mammary gland development and lactogenesis. *Genes and Dev.* 11, 179-186.
 - Ewald, D., Li, M., Efrat, S., Auer, G., Wall, R.J., Furth, P.A. and **Hennighausen, L.**(1996) Time-sensitive reversal of hyperplasia in transgenic mice expressing SV40 T antigen. *Science* 273, 1384-1386.
 - Liu, X.-W., Goulliaux, F., Robinson, G.W., Groner, B. and **Hennighausen, L.** (1995) Identification and characterization of STAT5 and a novel homologue (STAT5b) involved in prolactin mediated signal transduction in mouse mammary tissue. *Proc. Natl. Acad. Sci.U.S.A.* 92, 8831-8835.
 - Robinson, G.W., McKnight, R.A., Smith, G.H. and **Hennighausen, L.** (1995) Mammary epithelial cells undergo differentiation in cycling virgins but require pregnancy for the establishment of terminal differentiation. *Development* 121, 2079-2090.
 - Furth, P.A., St. Onge, L., Boger, H., Gruss, P., Gossen, M., Kistner, A., Bujard, H. and **Hennighausen, L.** (1994) Temporal control of gene expression in transgenic mice by a tetracycline responsive promoter. *Proc. Natl. Acad. Sci. U.S.A.* 91, 9302-9306.
 - Wall, R.J., Pursel, V.G., Shamay, A., McKnight, R.A., Pittius, C.W., and **Hennighausen, L.** (1991). High-level synthesis of a heterologous milk protein in the mammary glands of transgenic swine. *Proc. Natl. Acad. Sci. USA* 88, 1696-1700.
 - Burdon, T., Sankaran, L., Wall, R.J., Spencer, M., and **Hennighausen, L.** (1991). Expression of a whey acidic protein transgene during mammary development: Evidence for different mechanisms of regulation during pregnancy and lactation. *J. Biol. Chem.* 266, 6909-6914.
 - Gordon, K., Lee, E., Vitale, J.A., Smith, A.E., Westphal, H. and **Hennighausen, L.** (1987). Production of human tissue plasminogen activator in transgenic mouse milk. *BIO/TECHNOLOGY* 5, 1183-1187.
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 - **Hennighausen, L.** and Fleckenstein, B. (1986). Nuclear Factor 1 interacts with five DNA elements in the promoter region of the human cytomegalovirus major immediate early gene. *EMBO J.* 5, 1367-1371.
 - **Hennighausen, L.**, Siebenlist, U., Danner, D., Leder, P., Rawlins, D., Rosenfeld, P. and Kelly, T. (1985). High affinity binding site for a specific nuclear protein in the human IgM gene. *Nature* 314, 289-292.

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- **Hennighausen**, L.G. and Sippel, A.E. (1982). Characterization and cloning of the mRNAs specific for the lactating mouse mammary gland. *Eur. J. Biochem.* 125, 131-141.
 - **Hennighausen**, L.G. and Sippel, A.E. (1982). The mouse whey acidic protein is a novel member of the family of 'four-disulfide-core' proteins. *Nucleic Acids Res.* 10, 2677-2684.

Patents

- US # 5,831,141 Expression of a heterogeneous polypeptide in mammary tissue of mammals proteins in milk of transgenic animals
- US #5,998,382 Transfer of genes into tissue using jet injection
- US # 6,262,336 Expression of a heterogeneous protein C in mammary tissue of transgenic animals using the long WAP promoter
- US #6,361,991 Targeting gene expression to living tissue using jet injection
- EP #0264166B1 Production of foreign proteins in milk of transgenic animals