# Curriculum Vitae

**Name:** Thomas Henrik Bugge, Ph.D.

**Place of Birth:** Copenhagen, Denmark

**Citizenship:** Danish (U.S. Permanent Resident)

**Education:**

1989 M.Sc., Molecular Biology, The Institute of Microbiology, University of Copenhagen, Copenhagen, Denmark.

1993 Ph.D., Molecular Biology, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany.

**Brief Chronology of Employment:**

1987-1989 Pregraduate (M.Sc.) student, Laboratory of Tumor Virology, The Fibiger Institute, Copenhagen, Denmark.

1990-1993 Graduate studies in molecular biology, EMBL, Heidelberg, Germany.

1993-1995 Postdoctoral Fellow, The Finsen Laboratory, State University Hospital, Copenhagen, Denmark/ Children's Hospital Research Foundation, Cincinnati, Ohio.

1995-1996 Research Leader, The Finsen Laboratory, State University Hospital, Copenhagen, Denmark.

1997–1999 Associate Professor of Pediatrics, Children's Hospital Research Foundation, Cincinnati, Ohio.

1999–present Chief, Proteases and Tissue Remodeling Unit, Oral and Pharyngeal Cancer Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD.

**Honors and Other Special Scientific Recognition:**

1989 Pregraduate Fellowship, The Danish Cancer Society, Copenhagen, Denmark.

Predoctoral Fellowship, EMBL, Heidelberg, Germany.

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| | Travel Grant, The Danish Research Academy, Aarhus, Denmark. |
| | Travel Grant, The Danish Research Academy, Aarhus, Denmark. |
| | Fellowship, The Danish Cancer Research Foundation, Copenhagen, Denmark. |
| | Travel Grant, The Danish Plasmid Foundation, Glostrup, Denmark. |
| 1994 -1995 | Senior Researcher, The Danish Medical Research Council, Denmark. |
| 1996 | Received the "1996 Creativity Award" at the XIII$^{th}$ International Congress on Fibrinolysis and Thrombolysis, Barcelona, Spain. |
| 1999 | Abstract Selection Committee, “The First Meeting of the International Proteolysis Society”, Mission Point Resort, Mackinac Island, MI. |
| 1999 | Co-organizer, “The First Meeting of the International Proteolysis Society”, Mission Point Resort, Mackinac Island, MI. |
| 2002 | Discussion Moderator “Forbeck Symposium on Proteases as Cancer Therapeutic Targets” Captiva Island, FL. |
| 2002 | Scientific Advisory Board, “The Second Meeting of the International Proteolysis Society”, Munich, Germany. |
| 2002 | Session Chair, Proteolysis in Cancer, “The Second Meeting of the International Proteolysis Society”, Munich, Germany. |
| 2002 | Ad Hoc Reviewer, Promotion of Li Zhang to Associate Scientist, Department of Vascular Biology, American Red Cross, Rockville, M.D. |
| 2002 | Ad Hoc Reviewer, Promotion of Dr. Shijie Sheng, Department of Pathology, Wayne State University to Associate Professor with Tenure, Detroit, MI. |
| 2003 | Ad Hoc Reviewer, Promotion of Dr. Chen-Yong Lin, Lombardi Cancer Center, Georgetown University Medical Center. |
| 2003 | "NIDCR Staff Award" for Services to the National and International Research Communities. |
| 2003 | "NIDCR EEO Special Achievement Award" for "Extraordinary Initiative in Promoting Diversity and Career Development for Students and Fellows and Successfully Recruiting Underrepresented Minority Students". |

2004 Chair, Plenary Session I, XVIIth International Congress on Fibrinolysis and Proteolysis, Melbourne, Australia, (March 21-25, 2004).

2005 Organizer (with Dudley Strickland, Toni Antalis, and Dan Lawrence) "The Xth International Workshop on Molecular and Cellular Biology of Plasminogen Activation", Washington, D.C.

2005 Selected for NIH Director's Seminar Series, NIH, Bethesda, MD.

2006 International Organizing Committee, International Society for Fibrinolysis and Proteolysis Meeting, San Diego, August 27-31.

2006 Session Chair, Transmembrane Proteases/Extracellular Proteolysis, Gordon Conference on Plasminogen Activation and Extracellular Proteolysis. February 19-24, Ventura, CA.

2008 Vice Chair, Gordon Conference on Plasminogen Activation and Extracellular Proteolysis.

2010 Chair, Gordon Conference on Plasminogen Activation and Extracellular Proteolysis.

**Editorial Recognition of Research Publications**

1. Vassalli, J.-D. and Saurat, J. H. (1996). Cuts and scrapes? Plasmin heals! *Nature Medicine*, **2**, 284.

2. Mosesson. M. W. (2000). Fibrinogen as a determinant of the metastatic potential of tumor cells. *Blood*, **96**, 3301.

3. Pawlak, S. and Strickland, S. (2002). Tissue plasminogen activator and seizures: a clot-buster's secret life. *J. Clin. Invest.,* **109**,1529-1531.

4. Huchinson, E. (2003). Mass destruction. *Nature Reviews Cancer*, **3**, 82.

5. Brown, H. (2003). Engineered anthrax toxin has potent antitumour activity. *Lancet Oncology*, **4**, 64.

6. Herz, J. (2003). LRP: a bright beacon at the blood brain barrier. *J. Clin. Invest.,* **112**, 1483-1485.

7. Site-specific conversion of a pro-fusion protein toxin. (2004) *Blood*, **104**, 1919.

8. Tumors feed on collagen. (2005). J. Cell Biol. 169, 977-986.

9. Cancer: the matrix is now in control (2005) *Nature Medicine* **11** 1156-1159.

10. Journal Club (2005) *Nature* **438**, 534-535.

**Invited lectures and presentations since 1995:**

1. Bristol-Myers Squibb Lecture, Annual Meeting, Danish Cancer Research Society, Copenhagen, Denmark.

2. Plenary Lecture, 2nd Joint Meeting of the Wound Healing Society & The European Tissue Repair Society, Boston, MA.

3. Prize Lecture, XIIIth International Congress on Fibrinolysis and Thrombolysis, Barcelona, Spain.

4. 1996 Gordon Conference on Proteolytic Enzymes and their Inhibitors. New London, NH.

5. Seminar Speaker, The Danish Biological Society, Copenhagen, Denmark.

6. Seminar Speaker, Institute of Microbiology, University of Copenhagen, Copenhagen, Denmark.

7. Seminar Speaker, Tulane Medical School, Department of Biochemistry, New Orleans, LA.

8. Seminar Speaker, SUNY at Stony Brook, Department of Immunology and Pathology, Stony Brook, NY.

9. Seminar Speaker, Arris Pharmaceuticals, South San Francisco, CA.

10. Seminar Speaker, Uniklinik Freiburg, University of Freiburg, Freiburg, Germany.

11. Seminar Speaker, Differentiation Programme, EMBL, Heidelberg, Germany.

12. Seminar Speaker, State University Hospital, Copenhagen, Denmark.

13. Plenary Speaker, 17th International Congress of Biochemistry and Molecular Biology/American Society of Biochemistry and Molecular Biology, San Francisco, CA.

14. Seminar Speaker, Roche Bioscience, Palo Alto, CA.

15. Seminar Speaker, Affinity Group Seminar Series, Scripps Research Institute, San Diego, CA.

16. Seminar Speaker, Department of Vascular Biology, American Red Cross, Rockville, MD.

17. Seminar Speaker, The Burnham Institute, Department of Cell Adhesion-Extracellular Matrix Biology, San Diego, CA.

18. Seminar Speaker, "Molecular Medicine Seminar Series", University of Umea, Umea, Sweden.

19. Seminar Speaker, American Association for Cancer Research and ACTA Pathologica Microbiologica Immunologica Scandinavica meeting on "Proteases and Protease Inhibitors in Cancer", Nyborg, Denmark.

20. Seminar Speaker, State University Hospital, Copenhagen, Denmark.

21. Seminar Speaker, The National Institute of Dental and Craniofacial Research, The National Institutes of Health, Bethesda, MD.

22. Grand Rounds Speaker, Karmanos Cancer Institute, Wayne State University, Detroit, MI.

23. Speaker, Developmental Biology Protease Symposium, Wayne State University, Detroit, MI.

24. Speaker, Protease Consortium Meeting, Vanderbilt University, Nashville, TN.

25. Speaker, Melbourne Matrix Metalloproteinase Mini-Symposium, Melbourne, Australia.

26. Seminar Speaker, Craniofacial Development and Regeneration Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD.

27. Seminar Speaker, Oral Infection and Immunity Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD.

28. Seminar Speaker, Gene Therapy and Therapeutics Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD.

29. Seminar Speaker, Entremed, Rockville, MD.

30. Seminar Speaker, Novo/Nordisk A/S, Maaloev, Denmark.

31. Seminar Speaker, State University Hospital, Copenhagen, Denmark.

32. Seminar Speaker, Corvas International, Inc., San Diego, CA.

33. Seminar Speaker, Department of Vascular Biology, American Red Cross.

34. Seminar Speaker, Oral Infection and Immunity Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD.

35. Seminar Speaker, Laboratory of Cellular Carcinogenesis and Tumor Promotion, National Cancer Institute, Bethesda, MD.

36. Seminar Speaker, Lombardi Cancer Center, Georgetown University Medical Center, Washington, D. C.

37. Seminar Speaker, Gordon Conference on Proteolytic Enzymes and Their Inhibitors, New London, NH.

38. Seminar Speaker, American Association for Cancer Research, Proteases, Extracellular Matrix and Cancer, Hilton Head, SC.

39. Seminar Speaker, "Peptide Toxins Targeted to Cancer Symposium: Experience from animal studies and clinical trials". Copenhagen, Denmark.

40. Seminar Speaker, State University Hospital, Copenhagen, Denmark.

41. Speaker, National Cancer Institute-sponsored workshop on "Proteases and Cancer: Biology and Clinical Applications Workshop", Bethesda, MD.

42. Speaker, Immunology/Cell Biology Seminar series, NCI-Frederick, Frederick, MD.

43. Speaker, Celera, South San Francisco, CA.

44. Seminar Speaker, 47$^{th}$ Annual Meeting of the Society of Thrombosis and Haemostasis Research, Innsbruck, Austria.

45. Seminar Speaker, EMBL, Monterotondo, Italy.

46. Speaker, Laboratory of Cell Biology, National Heart Lung and Blood Institute, Bethesda, MD.

47. Seminar Speaker**,** 32$^{nd}$ Annual Meeting of Danish Society for Biochemistry and Molecular Biology.

48. Speaker, Gordon Conference on Plasminogen Activation and Extracellular Proteolysis. 2004, Ventura, CA

49. Plenary Speaker, XVIIth International Congress on Fibrinolysis and Proteolysis, Melbourne, Australia, (March 21-25, 2004).

50. Seminar Speaker, National Institute of Child Health, NIH, Bethesda, MD.

51. Invited speaker, Second Meeting of the American Society for Matrix Biology, San Diego, CA.

52. Seminar Speaker Department of Pharmacology, Wayne State University, Detroit, MI.

53. Seminar Speaker, Department of Pathology, Wayne State University, Detriot, MI.

54. NIH Director's Seminar Series, NIH, Bethesda, MD.

55. Seminar Speaker, Department of Cancer Biology, M. D. Anderson Cancer Center, Houston, TX.

56. Seminar Speaker, Department of Pharmacology, SUNY at Stony Brook, Stony Brook, NY

57. Speaker, Molecular Medicine Department, University of Michigan, Michigan, MI. 8/11/2005.

58. Speaker, Transmembrane Proteases/Extracellular Proteolysis, Gordon Conference on Plasminogen Activation and Extracellular Proteolysis. Ventura, CA. 2/21/06.

59. Speaker, Society of Biomolecular Screening, Baltimore, MD, 4/3/06.

60. Speaker, International Society for Fibrinolysis and Proteolysis Meeting, San Diego, August 27-31, 2006.

61. Speaker, Laboratory of Cell Biology, National Heart Lung and Blood Institute, September 14, 2006.

62. Key Note Speaker, 3rd Annual European Cancer Degradome Meeting, Nov. 7-9, 2006.

63. Speaker, Symposium Honoring the 70$^{th}$ Birthday of Professor Keld Danø, Nov 11, 2006.

**Grants**

1995-1996 Vera and Carl Johan Michaelsen Foundation Grant, " Investigation of the Molecular mechanisms of cancer invasion and metastasis by gene targeting", $ 20,000.

1997-1998 Board of Trustees Grant, Children's Hospital Research Foundation, "Determination of the role of the plasminogen activation system in cancer invasion and metastasis by tumor transplantation studies in plasminogen-deficient mice", $ 80,000.

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| 1997- 2001 | Danish Medical Research Council, “Transgenic molecular genetic analysis of the function and interaction of matrix degrading protease systems in tissue remodeling and cancer invasion”, $ 29,000. |
| 1998-2003 | NIH/NCI, RO1, CA79994-01, “Coagulation and Fibrinolysis in Tumor Progression”. (Initial Review Group Priority Score 133, Percentile 1.4) Total Direct Costs: $ 750,786. Grant relinquished after the transfer of research program to the NIH Intramural Program. |
| 1999-2001 | Supplement to NIH/NCI, RO1 CA79994-01, “Protease Consortium/Coagulation and Fibrinolysis in Tumor Progression.” Grant relinquished after the transfer of the research program to the NIH intramural program. |
| 1999 | Board of Trustees Grant, Children’s Hospital Research Foundation (extension), “Determination of the role of the plasminogen activation system in cancer invasion and metastasis by tumor transplantation studies in plasminogen-deficient mice”, $ 6,600. |
| 1999–2000 | NIH/NCI, R13, CA82133-01, (Co-investigator; P.I. Dr. B. F. Sloane) “Conference of the International Proteolysis Society.” Total Direct Costs: $ 7,500. |
| 2002–2005 | DOD/Breast Cancer Center of Excellence (Subcontract P.I.; P.I. Dr. B. F. Sloane) “Validation of Proteases as Therapeutic Targets in Breast Cancer: Functional Imaging of Protease Expression, Activity and Inhibition.” Total Direct Costs: $ 5,700,000. Subcontract PTRU $ 197,207. |
| 2003-2005 | NIAID Support of Intramural Biodefense Research from ICs other than NIAID,“ Imaging Anthrax Toxin Proteolytic Activation.” Total Direct Costs: $ 463,016. |
| 2005 | Imaging Probe Development Center (IPDC) Award, Molecular Imaging Roadmap Initiative. |
| 2006-2008 | NIAID Support of Intramural Biodefense Research from ICs other than NIAID,“ Anthrax Toxin Intoxication-Molecular Imaging and Identification of Novel Candidate Agents for Post-Exposure Treatment of Anthrax” Total Direct Costs: $ 498,782. |

**Administration**

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| 1999-present | Institutional Animal Care and Use Committee, NIDCR. |
| 1999-present | Gene Targeting Facility Oversight Committee, NIDCR. |

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| 1999-2003 | Animal Care Facility Oversight Committee, NIDCR. |
| 1999 | NIH Central Vivarium Animal Research Center Core Planning Committee |
| 2003 | NIDCR Veterinary Resources Core Contracts Technical Evaluation Panel. |
| 2004-present | Chair, Institutional Animal Care and Use Committee, NIDCR. |
| 2006 | Organizer, NIDCR Tenure-Track Seminar Series |
| 2006-present | Member, NIDCR Promotion and Tenure Committee. |

**Patents**

First Inventor:

"In vivo imaging of cell-surface protease activity using modified anthrax toxins." DHHS Ref No. E-295-01/0 (Co-inventors, Dr. Shi-Hui Liu, Dr. Stephen Leppla, and David Mitola). *Pending*

Co-inventor:

"Mutated anthrax toxin protective antigen proteins that specifically target cells containing high amounts of cell-surface metalloproteinases or plasminogen activator receptors." DHHS Ref No.E-293-99/1; PCT/US00/26192. First Inventor: Stephen Leppla. *Pending*

"Exploiting the Multimeric Nature of Certain Protein Toxins to Target Cells Having More than One Identifying Characteristic", First Inventor: Stephen Leppla. *Submitted*

"Activation of recombinant diphtheria toxin fusion proteins by specific proteases highly expressed on the surface of tumor cells", First Inventor: Stephen Leppla. *Submitted*

**Editorial Responsibilities**

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| 2002-present | Handling Editor, Thrombosis and Haemostasis |
| 2003-2005 | Editorial Board, Oral Oncology |
| 2005 | Guest Editor, Thrombosis and Haemostasis Theme Issue: Amalfi to Washington D.C. - Twenty Years of Plasminogen Activator Research. |
| 2005 | Editor, Proteases and Cancer, in Methods in Molecular Biology, Humana Press, USA |

2006 Editor, Frontiers in Bioscience, “Type II Transmembrane Serine Proteases” Issue

**Study Sections etc.**

2003 Ad Hoc Member, American Cancer Society, Cell Structure and Metastasis Committee.

2003 Congressionally Directed Medical Research Programs, Prostate Cancer Research Program, Pathobiology-2.

2004 Regular Member, American Cancer Society, Cell Structure and Metastasis Committee.

2004 Ad Hoc reviewer, The Telethon Foundation, Italy

2005 Ad Hoc Reviewer, German Research Council, “Tumor Vessel Interface” Priority Program

2006 NCI sponsored Think Tank: Imaging Tumors and Their Microenvironment, June 8–10, 2006, Alexandria, Virginia

2006 Ad Hoc Reviewer, Austrian Science Fund.

**Ad Hoc Journal Review**

AfCS-Nature Signaling Gateway

American Journal of Pathology

American Journal of Respiratory Cell and Molecular Biology

Arthritis and Rheumatism

Bioorganic & Medicinal Chemistry Letters

Blood

Cancer Research

Circulation

Clinical Cancer Research

Developmental Cell

EMBO Journal

International Journal of Cancer

Journal of the National Cancer Institute

Journal of Investigative Dermatology

Molecular and Cellular Biology

Molecular Carcinogenesis

Neoplasia

Nature Genetics

Nature Medicine

Nature Reviews Microbiology

Oncogene

Proceedings of the National Academy of Sciences (USA)

The Journal of Biological Chemistry

The Journal of Cell Biology

The Journal of Cellular Biochemistry

The Journal of Cell Science

The Journal of Clinical Investigation

The Journal of Clinical Pathology

The Journal of Histochemistry and Cytochemistry

Thrombosis and Haemostasis

The Journal of Immunology

Trends in Cardiovascular Medicine

**Bibliography**

1) Andreassen, H., Bohr, H., Bohr, J., Brunak, S., Bugge, T., Cotterill, R. M., Jacobsen, C., Kusk, P., Lautrup, B., Petersen, S. B., Sæhrmark, T., and Ulrich, K. (1990). Analysis of the secondary structure of the human immunodeficiency virus (HIV) proteins p17, gp120, and gp41 by computer modeling based on neural networks methods. *J. Acquir. Immune. Defic. Syndr.,* 6, 615-622.

2) Bugge, T. H., Lindhardt, B. Ø., Hansen, L. L., Kusk, P., Hulgaard, E. F., Holmbäck, K., Klasse, P. J., Zeuthen, J., and Ulrich, K. (1990). Analysis of a highly immunodominant epitope in the human immunodeficiency virus type 1 transmembrane glycoprotein, gp41, defined by a human monoclonal antibody. *J. Virol.*, **64**, 4123-4129.

3) Bugge, T. H., Hansen, L. L., Lindhardt, B. Ø., Kvinesdal, B., Kusk, P., Holmbäck, K., Hulgaard, E. F., and Ulrich K. (1991). Competition ELISA using a human monoclonal antibody for the detection of antibodies against human immunodeficiency virus type 1. *J. Virol. Methods*, **32**, 1-10.

4) Kusk, P., Bugge, T. H., Lindhardt, B. Ø., Hulgaard, E. F., and Holmbäck, K. (1992). Mapping of linear B-cell epitopes on the major core protein p24 of human immunodeficiency virus type 1 (HIV-1). *AIDS Res. Hum. Retroviruses,* **8**, 1789-1794.

5) Kusk, P., Lindhardt, B. Ø., Bugge, T. H., Holmbäck, K., and Hulgaard, E. F. (1993). Mapping of a new immunodominant human linear B-cell epitope on the vpu protein of the human immunodeficiency virus type 1. *J. Acquir. Immune. Defic. Syndr.*, **6**, 334-338.

6) Holmbäck, K., Kusk, P., Hulgaard, E. F., Bugge, T. H., Scheibel, E., and Lindhardt, B. Ø. (1993). Autologous antibody response against the principal neutralizing domain of human immunodeficiency virus type 1 isolated from infected humans. *J. Virol.,* **67***,* 1612-1619.

7) Kusk, P., Holmbäck, K., Lindhardt, B. Ø., Hulgaard, E. F., and Bugge, T. H. (1992). Mapping of two new human B-cell epitopes on HIV-1 gp120. *AIDS*, **6**, 1451-1456.

8) Disela, C., Glineur, C., Bugge, T., Sap, J., Stengl, G., Dodgson, J., Stunnenberg, H. G., Beug, H., and Zenke, M. (1991). v-erbA overexpression is required to extinguish c-erbA function in erythroid cell differentiation and regulation of the erbA target gene CA II. *Genes & Dev.*, **5**, 2033-2047.

9) Vivanco-Ruiz, M. M, Bugge, T. H., Hirchmann, P., and Stunnenberg H. G. (1991). Functional characterization of a natural retinoic acid responsive element. *EMBO J.*, **10**, 3829-3838.

10) Bugge, T. H., Pohl, J., Lonnoy, O., and Stunnenberg, H. G. (1992). RXR$\alpha$, a promiscuous partner of retinoic acid and thyroid hormone receptors. *EMBO J.*, **11**, 1409-1418.

11) Barettino, D., Bugge, T. H., Bartunek, P., Vivanco-Ruiz, M. D., Sonntag-Buck, V., Beug, H., Zenke, M., and Stunnenberg, H. G. (1993). Unliganded $T_3R$, but not its oncogenic variant v-erbA suppresses RAR dependent transactivation by titrating out RXR. *EMBO J.*, **12**, 1343-1354.

12) Islam, T. C., Bugge, T. H., and Bohm, S. (1993). The long terminal repeat of VL30 retrotransposons contains sequences that determine retinoic acid-induced transcription in cultured keratinocytes. *J. Biol. Chem.*, **268**, 3251-3259.

13) Bugge, T. H., Flick, M. J., Daugherty, C. C., and Degen, J. L. (1995). Plasminogen deficiency causes severe thrombosis but is compatible with development and reproduction. *Genes & Dev.*, **9**, 794-807.

14) Bugge, T. H., Suh, T. T., Flick, M. J., Daugherty, C. C., Rømer, J., Solberg, H., Ellis, V., Danø, K., and Degen, J. L. (1995). The receptor for urokinase-type plasminogen activator is not essential for mouse development or fertility. *J. Biol. Chem.,* **270**, 16886-16894.

15) Rømer, J., Bugge, T. H., Pyke, C., Lund, L. R., Flick, M. J., Degen, J. L., and Danø, K. (1996). Impaired wound healing in mice with a disrupted plasminogen gene. *Nature Medicine,* **2**, 287-292.

16) Rømer, J., Bugge, T. H., Pyke, C., Lund, L. R., Flick, M. J., Degen, J. L., and Danø, K. (1996). Plasminogen and wound healing (Letter to the editor). *Nature Medicine,* **2**, 725.

17) Bugge, T. H., Flick, M. J., Danton M. J., Daugherty, C. C., Rømer, J., Danø, K., Carmeliet, P., Collen, D., and Degen J. L. (1996). Urokinase-type plasminogen activator is effective in fibrin clearance in the absence of its receptor or tissue-type plasminogen activator. *Proc. Natl. Acad. Sci. (USA),* **93**, 5899-5904.

18) Bugge, T. H., Xiao, Q., Kombrinck, K. W., Flick, M. J., Holmbäck, K., Danton, M. J., Colbert, M. C., Witte, D. P., Fujikawa, K., Davie, E. W., and Degen, J. L. (1996). Fatal embryonic bleeding events in mice lacking tissue factor, the cell-associated initiator of blood coagulation. *Proc. Natl. Acad. Sci. (USA),* **93**, 6258-6263.

19) Bugge, T. H., Kombrinck, K., Flick, M. J., Daugherty, C. C., Danton, M. J., and Degen J. L. (1996). Loss of fibrinogen rescues mice from the pleiotropic effects of plasminogen deficiency. *Cell,* **87**, 709-719.

20) Tsirka, S. E., Rogove, A. D., Bugge, T. H., Degen, J. L., and Strickland, S. (1997). An extracellular proteolytic cascade promotes neuronal degeneration in the mouse hippocampus. *J. Neurosci.,* **17**, 543-552.

21) Coleman, J. L., Gebbia, J. A., Piesman, J., Degen, J. L., Bugge, T. H., and Benach, J. L. (1997). Plasminogen is required for efficient dissemination of *Borrelia burgdorferi*

in ticks and for enhancement of spirochetemia in the vertebrate host. *Cell,* **89**, 1111-1119.

22) Tsirka, S. E., Bugge, T. H., Degen, J. L., and Strickland, S. (1997). Neuronal death in the central nervous system demonstrates a non-fibrin substrate for plasmin. *Proc. Natl. Acad. Sci. (USA),* **94**, 9779-9781.

23) Xiao, Q., Danton, M. J., Witte, D. P., Kowala, M. C., Valentine, M. T., Bugge, T. H., and Degen, J. L. (1997). Plasminogen-deficiency accelerates vessel wall disease in mice predisposed to atherosclerosis. *Proc. Natl. Acad. Sci. (USA),* **94**, 10335-10340.

24) Bugge, T. H., Kombrinck, K. W., Xiao, Q., Holmbäck, K., Daugherty, C. C., Witte, D. P., and Degen, J. L. (1997). Growth and dissemination of Lewis lung carcinoma in plasminogen-deficient mice. *Blood,* **90**, 4522-4531.

25) Kao, W.-Y., Kao, C. W., Kaufman, A. H., Kombrinck, K. W., Converse, R. L., Good, W. V., Bugge, T. H., and Degen, J. L. (1998). Healing of corneal epithelial defects in plasminogen and fibrinogen-deficient mice. *Investigative Ophthalmology & Visual Science,* **39**, 502-508.

26) Drew, A. F., Kaufman, A. H., Kombrinck, K. W., Danton, M. J., Daugherty, C. C., Degen, J. L., and Bugge, T. H. (1998). Ligneous conjunctivitis in plasminogen-deficient mice. *Blood,* **91**, 1616-1624.

27) Bugge, T. H., Lund, L. R., Kombrinck, K. W., Nielsen, B. S., Holmbäck, K., Drew, A. F., Flick, M. J., Witte, D. P., Danø, K. and Degen, J. L. (1998). Reduced metastasis of Polyoma virus middle T antigen-induced mammary cancer in plasminogen-deficient mice. *Oncogene,* **16**, 3097-3104.

28) Sun, Y. W., Witte, D. P., Degen, J. L., Colbert, M. C., Burkart, M. C., Holmbäck, K., Xiao, Q., Bugge, T. H., and Degen, S. J. (1998). Prothrombin deficiency results in embryonic and neonatal lethality in mice. *Proc. Natl. Acad. Sci. (USA),* **95**, 7597-7602.

29) Busso, N., Péclat, V., Van Ness, K., Kolodziesczyk, E., Degen, J. L., Bugge, T., and So, A. (1998). Exacerbation of antigen-induced arthritis in urokinase-deficient mice. *J. Clin. Invest.,* **102**, 41-50.

30) Bugge, T. H., and Degen, J. L. (1998). Plg. In *The Gene Knockout FactsBook.* (eds. Mak, T. W., Penninger, J., Roder, J., Rossant, J., and Sounders, M.), Academic Press, San Diego, CA. p876-877.

31) Bugge, T. H., and Degen, J. L. (1998). uPAR. In *The Gene Knockout FactsBook.* (eds. Mak, T. W., Penninger, J., Roder, J., Rossant, J., and Sounders, M.), Academic Press, San Diego, CA p1061-1062.

32) Bugge, T. H., and Degen, J. L. (1998). Tissue factor. In *The Gene Knockout FactsBook.* (eds. Mak, T. W., Penninger, J., Roder, J., Rossant, J., and Sounders, M.), Academic Press, San Diego, CA p1010-1011.

33) Gebbia, J. A., Monco, J. C., Degen, J. L., Bugge, T. H., and Benach, J. L. (1999). The plasminogen activation system enhances brain and heart invasion in murine relapsing fever Borreliosis. *J. Clin Invest.,* **103**, 81-87*.*

34) Chen, Z.L, Indyk, J. A., Bugge, T. H., Kombrinck, K. W., Degen, J. L., and Strickland, S. (1999). Neuronal death and blood-brain barrier breakdown after excitotoxic injury are independent processes. *J. Neurosci.*, **19**, 9813-9820.

35) Lund, L. R., Rømer, J., Bugge, T. H., Nielsen, B. S., Frandsen, T. L., Degen, J. L., Stephens, R. W., and Danø, K. (1999). Functional overlap between two classes of matrix-degrading proteases in wound healing. *EMBO J.* **18***,* 4645-4656.

36) Bezerra, J. A., Bugge, T. H., Melin-Aldana, H., Sabla, G., Kombrinck, K. W., Witte, D. P., and Degen, J. L. (1999). Plasminogen deficiency leads to impaired remodeling after a toxic injury to the liver. *Proc. Natl. Acad. Sci. (USA),* **96***,* 15143-15148.

37) List, K., Jensen, O. N., Bugge, T. H., Lund, L. R., Ploug, M., Danø, K., and Behrendt, N. (2000). Plasminogen-independent initiation of the pro-uPA activation cascade *in vivo*. Activation of pro-urokinase by glandular kallikrein (mGK-6) in plasminogen-deficient mice. *Biochemistry,* **39**, 508-515*.*

38) Drew, A. F., Schiman, H. L., Kombrinck, K. W., Bugge, T. H., Degen, J. L., and Kaufman, A. H. (2000). Persistent corneal haze after excimer laser photokeratectomy in plasminogen-deficient mice. *Invest. Ophthalmol. Vis. Sci*. **41**, 67-72*.*

39) Wu, Y. P., Siao, C. J., Lu, W., Sung, T. C., Frohman, M. A., Milev, P., Bugge, T. H., Degen, J. L., Levine, J. M., Margolis, R. U., and Tsirka, S. E. (2000). The tissue plasminogen activator (tPA)/plasmin extracellular proteolytic system regulates seizure-induced hippocampal mossy fiber outgrowth through a proteoglycan substrate. *J. Cell Biol.,* **148**, 1295-1304.

40) Lund, L. R., Bjørn, S. F., Sternlicht, M. D., Nielsen, B. S., Solberg, H., Usher, P. A., Østerby, R., Christensen, I. J., Stephens, R. J., Bugge, T. H., Danø, K., and Werb, Z. (2000). Lactational competence and involution of the mouse mammary gland require plasminogen. *Development,* **127**, 4481-4492.

41) Goguen, J. D., Bugge, T., and Degen, J. L. (2000). Role of the pleiotropic effects of plasminogen deficiency in infection experiments with plasminogen-deficient Mice. *Methods*, **21**, 179-183.

42) Drew, A. F., Tucker, H. L., Kombrinck, K. W., Simon, D. I., Bugge, T. H., and Degen, J. L. (2000). Plasminogen is a critical determinant of vascular remodeling in mice. *Circulation Research*, **87**, 133-139.

43) Palumbo, J. S., Kombrinck, K. W., Drew, A. F., Grimes, T. S., Kiser, J. H., Degen, J. L., and Bugge, T. H. (2000). Fibrinogen is an important determinant of the metastatic potential of circulating tumor cells. *Blood,* **96**, 3302-3309.

44) Bezerra, J. A., Currier, A. R., Melin-Aldana, H., Sabla, G., Bugge, T. H., Kombrinck, K. W., and Degen, J. L. (2001). Plasminogen Activators Direct Reorganization of the Liver Lobule after Acute Injury. *Am. J. Pathol.*, **158**, 921-929.

45) Liu, S., Bugge, T. H., and Leppla, S. H. (2001). Targeting tumor cells by urokinase plasminogen activator-activated anthrax toxin protective antigens. *J. Biol. Chem.* **276**,17976-17984.

46) Engelholm, L. H., Nielsen, B. S., Netzel-Arnett, S., Solberg, H., Chen, X. D., Lopez Garcia J.M., Lopez-Otin, C., Young, M. F., Birkedal-Hansen, H., Danø, K., Lund, L. R., Behrendt, N., and Bugge, T. H. (2001). The urokinase plasminogen activator receptor-associated protein/Endo 180 is coexpressed with its interaction partners uPAR and matrix metalloproteinase-13 during osteogenesis. *Lab. Invest.* **81**, 1403-1414.

47) Yepes, M., Sandkvist, M., Coleman, T. A., Moore, E., Wu, J.-Y., Mitola, D., Bugge, T. H., and Lawrence, D. (2002). Regulation of seizure spreading by neuroserpin and tissue plasminogen activator is plasminogen-independent. *J.Clin. Invest.* **109**, 1571-1578.

48) Bugge, T. H. (2002). Proteolysis in carcinogenesis. In “Head and Neck Cancers”, *Eds.* Gutkind, J. S., Jacobs J. R., and Lippman, S. M., Academic Press, San Diego, CA.

49) Frankel. A. E., Bugge, T. H., Liu, S., Vallera, D. A., and Leppla, S. H. (2002). Peptide toxins directed at matrix dissolution systems of cancer cells. *Protein and Peptide Lett.*, **9**, 1-14.

50) List, K., Haudenschild, C. C., Szabo, R., Chen, W., Wahl, S. M., Swaim, W., Engelholm, L. H., Behrendt, N., and Bugge, T. H. (2002). Matriptase/MT-SP1 is required for postnatal survival, epidermal barrier function, hair follicle development, and thymic homeostasis. *Oncogene*, **21**, 3765-3779.

51) Bannach, F. G., Gutierrez, A., Fowler, B. J., Bugge, T. H., Degen, J. L., Parmer, R. J., and Miles, L. A. (2002). Localization of regulatory elements mediating constitutive and cytokine-stimulated plasminogen gene expression. *J. Biol. Chem.* **277**, 38579-38588.

52) Netzel-Arnett, S. A., Mitola, D. J., Yamada, S., Chrysovergis, K., Holmbeck, K., Birkedal-Hansen, H. and Bugge, T. H. (2002). Collagen Dissolution by Keratinocytes Requires Cell Surface Plasminogen Activation and Matrix Metalloproteinase Activity. *J. Biol. Chem.*, **277**, 45154-45161.

53) Curino, A., Mitola, D., Aaronson H., McMahon, G., Raja, K., Keegan, A., Lawrence, D. A, and Bugge, T. H. (2002). Plasminogen promotes sarcoma growth and suppresses the accumulation of tumor-infiltrating macrophages. *Oncogene*, **21**, 8830-8842.

54) Montaner, S., Sodhi, A., Molinolo, A., Bugge, T. H., Sawai, E. T., He, Y., Li, Y., Ray, P. E., and Gutkind, J. S. (2003). Endothelial infection with KSHV genes in vivo reveals that vGPCR initiates Kaposi's sarcomagenesis and can promote the tumorigenic potential of viral latent genes. *Cancer Cell*, **3**, 23-36.

55) Liu, S., Aaronson, H., Mitola, D., Leppla, S. H., and Bugge, T. H. (2003). Potent anti-tumor activity of a urokinase-activated engineered anthrax toxin. *Proc. Natl. Acad. Sci. (USA)*, **100**, 657-662.

56) Netzel-Arnett, S., Hooper, J. D., Szabo, R., Madison, E. L., Quigley, J. P., Bugge, T. H. and Antalis, T. M. (2003). Membrane Anchored Serine Proteases: An emerging class of cell surface proteolytic enzymes with potential roles in cancer. *Cancer and Metastasis Reviews*, **22**, 237-258.

57) Engelholm, L. H., List, K., Netzel-Arnett, S., Cukierman, E., Mitola, D. J., Aaronson, H., Kjøller, L., Larsen, J. K., Yamada, K. M., Strickland, D. S., Holmback, K., Danø, K., Birkedal-Hansen, H., Behrendt, N., and Bugge T. H. (2003). uPARAP/Endo180 is essential for cellular uptake of collagen and promotes fibroblast collagen adhesion. *J. Cell Biol.*, **160**, 1009-1015.

58) Pedersen, T. X., Leethanakul, C, Patel V, Mitola, D. J., Lund, L.R., Danø, K., Johnsen, M., Gutkind, J. S., and Bugge, T. H. (2003). Laser capture microdissection-based *in vivo* genomic profiling of wound keratinocytes identifies similarities and differences to squamous cell carcinoma. *Oncogene*, **22**, 3964-3976.

59) Szabo, R., Qingyu Wu, Q., Dickson, R. B., Netzel-Arnett, S, Antalis, T. M., and Bugge, T. H. (2003). Type II Transmembrane Serine Proteases. *Thrombosis and Haemostasis*, **90**, 185-193.

60) Liu, S. Schubert, R. L. Bugge, T. H., and Leppla, S. H. (2003). Anthrax toxin: structures, functions, and tumor targeting. *Expert Opin. Biol. Ther.*, **3**, 843-853.

61) Makarova, A., Mikhailenko, I, Bugge, T. H., List, K. Lawrence, D, and Strickland, D. K. (2003). The LDL receptor-related protein modulates protease activity in the brain by mediating the cellular internalization of both neuroserpin and neuroserpin:tPA complexes. *J. Biol. Chem.*, **278**, 50250-50258.

62) Frankel, A. F., Neville, D. M., Bugge, T.H., Kreitman, R. J., Leppla, S. H. (2003) Immunotoxin therapy of hematologic malignancies. *Semin Oncol.*, **30**, 545-557.

63) Yepes, M., Sandkvist, M., Moore, E., Bugge, T.H., Strickland, D. K., and Lawrence, D. (2003). Tissue-type plasminogen activator opens the blood brain barrier via the low density lipoprotein receptor. *J. Clin. Invest.,* **112**, 1533-1540.

64) List, K., Szabo, R., Wertz, P.W., Segre, J., Haudenschild, C. C., Kim, S.-Y., and Bugge, T. H. (2003). Loss of proteolytically processed filaggrin caused by epidermal deletion of Matriptase/MT-SP1. *J. Cell Biol.*, **163**, 901-910.

65) Riedlinger, G., Kridel, S., Al-Housseini, A.,Gardner, L., Bugge, T. H., Leppla, S. H., Duesbery, N., Vande Woude, G., and Frankel, A. (2003). Metastatic melanoma and matrix metalloproteases. *Drugs of the Future*, **28**, 897-904.

66) Kjøller, L., Engelholm, L., Høyer-Hansen, M., Danø, K., Bugge, T. H., and Behrendt, N. (2004). uPARAP/endo180 directs lysosomal delivery and degradation of collagen. *Exp. Cell. Res.*, **293**, 106-116.

67) Law, B., Curino, A., Bugge, T.H., Weissleder, R., and Tung, C. H. (2004). Design, synthesis and characterization of urokinase-type plasminogen activator sensitive near-infrared reporter. *Chem. Biology*, **11**, 99-106.

68) Abi-Habib, R. J., Liu, S., Bugge, T. H., Leppla, S., H., and Frankel, A. E. (2004). Urokinase activated recombinant diphtheria toxin targeting the granulocyte-macrophage colony-stimulating factor receptor (dtu2gmcsf) is selectively cytotoxic to human acute myeloid leukemia blasts. *Blood*, **104**, 2143-2148.

69) Curino, A., Patel, V., Nielsen, B. S., Iskander, I. J., Ensley, J. F., Yoo, G. H., Holsinger, F. C., Myers, J. N., El-Nagaar, A., Kellman, R, Shillitoe, E. J., Molinolo, A. A., Gutkind, J. S., and Bugge, T. H. (2004) Detection of uPA activity in oral cancer by laser capture microdissection combined with plasminogen-casein zymography. *Oral Oncology*, **40**, 1026-1032.

70) Hobson, J. P., Netzel-Arnett, S., Szabo, R., Rehault, S. M., Church F. C., Strickland, D. K., Lawrence, D. A., Antalis, T. M. and Bugge, T. H. (2004) Mouse DESC1 is located within a cluster of seven DESC1-like genes and encodes a type II transmembrane serine protease that forms serpin inhibitory complexes. *J. Biol. Chem.*,**279**, 46981-46994.

71) Law, B., Hsiao, J.-K., Bugge, T. H., Weissleder, R., Tung, C.-H. (2004). Novel optical zymography for the detection of urokinase plasminogen activator in biological samples, *Analytical Biochemistry*, **338**, 151-158.

72) Westcott. M. M., Abi-Habib, R., Cohen, K., Willingham, M., Vallera, D., Liu, S., Bugge, T. H., Leppla, S. H., and Frankel, R. (2004). Diphtheria toxin-murine GMCSF-induced hepatotoxicity is mediated by Kupffer cells. *Mol. Cancer Ther.*, **3**,1681-1689.

73) Antalis, T.M., Bugge, T.H., Lawrence, D. A., Netzel-Arnett, S., Schwartz, B. S., Strickland, D. K. (2005). Amalfi to Washington D.C. - Twenty Years of Plasminogen Activator Research. *Thrombosis and Haemostasis*, **93**, 625-626.

74) Szabo, R., Netzel-Arnett, S., Hobson, J. P., Antalis, T. M., and Bugge, T. H., (2005). Matriptase-3 is a novel phylogenetically preserved membrane-anchored serine protease with broad serpin reactivity. *Biochemistry*, **390**, 231-242.

75) Liu, S., Redeye, V., Kuremsky, J. G., Bugge, T. H., and Leppla, S. H. (2004). Intermolecular complementation achieves high-specificity tumor targeting by anthrax toxin. *Nature Biotechnology*, **23**, 725-730.

76) Curino, A. C., Nielsen, B. S., Engelholm, L. H., Molinolo, A. A., Behrendt, N., and Bugge, T. H. (2005). Intracellular collagen degradation mediated by uPARAP/Endo180 is a major pathway of extracellular matrix turnover during malignancy. *J. Cell Biol.* **169**, 977-986.

77) List, K., Szabo, R., Molinolo, A., Sriuranpong, V., Redeye, V., Burke B., Murdock, T., Nielsen, B.S., Gutkind, J.S., and Bugge, T. H. (2005). Deregulated matriptase proteolysis causes ras-independent multistage carcinogenesis and promotes ras-mediated malignant transformation. *Genes & Dev.*, **19**, 1934-1950.

78) Filippov, S., Chun, T.-H., Hotary, K. B., Ota, I., Allen, E. D., Bugge, T.H., Birkedal-Hansen, H., Holmbeck, K., Fay, W., and Weiss, S.J. (2005). MT1-MMP deficiency suppresses vascular neointimal lesion formation. *J. Exp. Med,* **202**, 663-671.

79) Rønø, B., Rømer, J., Liu, S., Bugge, T. H., Leppla, S. H., and Kristjansen, P. E. (2005). Significant antitumor efficacy after systemic administration of urokinase activation-dependent anthrax toxin. *Molecular Cancer Therapeutics*, **5**, 89-96.

80) Bugge, T.H. and Leppla, S. H. (2006) Anthrax target in macrophages pinpointed. *Nature Genetics*, **38**, 137-138.

81) List, K., Szabo, S., Molinolo, A., Nielsen, B. S., and Bugge, T. H. (2006). Delineation of matriptase protein expression by enzymatic gene trapping suggests diverging roles in barrier function, hair formation, and squamous cell carcinogenesis. *Am. J. Pathol.*, **168**, 1513-1525.

82) Hobson, J. P., Liu S., Rønø, B., Leppla, S. H., and Bugge, T.H. (2006). Imaging specific cell surface proteolytic activity in single living cells. *Nature Methods*, **3**, 259 – 261.

83) List, K., Bugge, T. H., and Szabo (2006). Matriptase: Potent proteolysis of the cell surface. *In press, Molecular Medicine*.

84) Szabo, R., Molinolo, A., List, K., and Bugge, T. H. (2006). Matriptase is the essential target of hepatocyte growth factor activator inhibitor-1 during embryonic development. *In press, Oncogene*.

85) Abi-Habib, R. J., Singh, R., Liu, S., Bugge, T. H., Leppla, S. H., and Frankel, A. E. (2006). A Urokinase Activated Recombinant Anthrax Toxin Is Selectively Cytotoxic to Many Different Tumors. *In press, Molecular Cancer Therapeutics*.

86) Schwartz, D. R., Moin, K., Yao, B, Matrisian, L. M, Coussens, L. M., Bugge, T. H., Fingleton, B., Acuff, H. B., Sinnamonm M., Nassar, H. Krawetz, B., Linebaugh, B., and Sloane, B. F. (2006). The Hu/Mu ProtIn oligonucleotide microarray: application of a custom dual species array for mining protease, protease inhibitor and protease interactor gene expression in tumors and their microenvironment. *Submitted*.

87) Netzel-Arnett S., Currie, B. M., Szabo, R., Lin, C. Y., Chen, L M., Chai K. X., Antalis, T. M., Bugge, T. H., and List, K. (2006) Evidence for a matriptase-prostasin proteolytic cascade regulating terminal epidermal differentiation. *In Press, J. Biol. Chem.*