CURRICULUM VITAE

Randell T. Libby

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Education

Ph.D., Molecular Genetics, Oregon State University, 1981.
M.S., Microbial Genetics, California State University, 1977.
B.S., Animal Science/Physiology, University of California-Davis, 1974.

Professional Experience

Affiliate, Translational Research Program, Section of Neurology, Benaroya Research Institute, Virginia Mason Medical Center, Seattle, Washington 98101 (2009 – present)

*Senior (Faculty) Research Associate***,** School of Medicine, Department of Laboratory Medicine, University of Washington (2003 – 2009)

Senior Fellow, School of Medicine, Department of Laboratory Medicine, University of Washington, 1998 – 2003.

Affiliate, School of Medicine, Center for Human Health and Disability, Division of Medical Genetics, University of Washingto, 2001-present.

Resident Consultant, Department of Pathobiology and Molecular Biology, NeoRx Pharmaceutical Corporation, 1994 - 2000.

Visiting Scholar, Department of Genetics, University of Washington, 1993 - 1994.

Research Assistant Professor, Department of Genetics, University of Washington, 1990 - 1992.

*Research Associate***,** Department of Genetics, University of Washington, 1987 - 1989.

Visiting Fellow, Department of Cellular & Molecular Biology, Institut Jacques Monod, Universite de Paris VII, 1989.

Staff Scientist, Department of Molecular Biology, Immunex Corporation, 1984 - 1987.

Senior Research Associate, Department of Microbiology, The Ohio State University, 1982 - 1984.

Visiting Research Fellow, Department of Public Health & Microbiology, Michigan State University, 1981.

Visiting Research Fellow, Department of Microbiology, University of Iowa, 1981.

Postdoctoral Research Associate, Department of Microbiology, The Ohio State University, 1980 - 1982.

Predoctoral Research Assistant, Department of Microbiology, Oregon State University, 1978 - 1980.

Teaching Assistant, Department of Microbiology, Oregon State University, 1976 - 1978.

Teaching Assistant, Department of Microbiology, California State University, 1974 -1975.

Reviewer

Biochemistry Journal, 1987 - present.

Research Support

National Institutes of Health (GM 59356), Triplet Repeat Instability, Albert R. LaSpada, P.I. and Randell T. Libby, Senior Research Associate, 1998-present.

National Institutes of Health (No. 13626-22), Control of Cell Growth, Jonathan A. Gallant, P.I. and Randell T. Libby, Research Assistant Professor, 1990 - 1992.

American Cancer Society (No. NP279H), Regulatory Nucleotides, Jonathan A. Gallant, P.I. and Randell T. Libby, Research Associate, 1988 - 1989.

National Research Service Awardee (No. 5 T32 AG00057-10 0071), Mechanisms of Error Reduction, Randell T. Libby, Research Associate. 1986 - 1987.

National Institutes of Health (No. R01-AG01546), Protein Stability & Aging in Anucleate Cells, John N. Reeve, P.I., and Randell T. Libby, Research Associate, 1980 - 1982.

Environmental Protection Agency (No. N0237093), Application of Recombinant DNA Technology to Methane Biogenesis, John N. Reeve, P.I., and Randell T. Libby, Senior Research Associate, 1982 - 1984.

Major Research Interest

Molecular Neurogenetics: Molecular mechanisms of triplet repeat instability and neurotoxicity in the development of neurodegenerative disorders. Translational therapy in sporadic Amyotrophic Lateral Sclerosis (sALS).

Gene Therapy: development of non-viral gene therapy strategies for the treatment of vascular smooth muscle cell proliferation.

Postdoctoral Research

University of Washington: Efforts have been directed towards identifying novel regulatory pathways required for the avoidance and correction of transcriptional errors.

The Ohio State University: Components of the transcription/translation apparatus prone to increased error frequency upon senescence were identified. An error catastrophe theory, due to the mistranslation of the early genes involved in *T7* development were established, and mechanisms whereby proteins are inactivated was investigated.

Additional studies were directed towards an examination of promoter structures in Archaebacterial DNA: the terminal enzyme in the methane biosynthetic pathway was cloned and expressed in *Escherichia coli*.

Predoctoral Research

Oregon State University: The RNA polymerase from *Bacillus subtilis* was purified, and its enzymatic activities characterized. The regulation of synthesis of the individual subunits of the enzyme were established.

California State University: Transformation of auxotrophic markers from *E. coli* were used to compliment equivalent lesions in yeast through the construction of *E. coli*/yeast shuttle vectors.

Scientific Affiliations

American Society of Human Genetics
Genetics Society of America
American Society for Microbiology
American Association for the Advancement of Science
New York Academy of Sciences
The RNA Society
The American Society of Gene Therapy
American Academy of Forensic Sciences
Society for Neuroscience

Awards and Honors

Wood/Whelan Fellowship: International Union of Biochemistry (1989), Universite de Paris VII.

National Research Service Awardee: Regulation of Transcriptional Fidelities, 1986 - 1987.

Hughes Scholarship: Regulation of Transcription in *Bacillus subtilis,* 1978.

Patents

PCT International Patent: Delivery Vehicles for Bioactive Agents and Uses Therof, Randell T. Libby, Lawrence L. Kunz, Thomas R. Tice, and Christopher W. McDaniel, PCT WO 99/21533

U.S. Patent Application: Delivery Vehicles for Bioactive Agents and Uses Therof, Randell T. Libby, Lawrence L. Kunz, Thomas R. Tice, and Christopher W. McDaniel, U.S. Patent No. 09/178,438

***Scholarly Activities (Selected List)*:**

Publications

Sporadic ALS has compartment-Specific Aberrant Exon Splicing and Altered Cellmatrix Adhesion Biology. Stuart Rabin, Hugo Kim, Michael Baughn, Ryan T. Libby, Young Joo Kim, Yuxin Fan, Randell T. Libby, Albert La Spada, Brad Stone and John Ravits. Human Molecular Genetics: October 28, 2009 (Advanced On-Line Publication), doi: 10.1093/hmg/ddp498

CTCF *Cis*-Regulates Trinucleotide Repeat Instability in an Epigenetic Manner: A Novel Basis for Mutational Hot Spot Determination. Randell T. Libby, Katherine Hagerman, Victor V. Pineda, Rachel Lau, Diane H. Cho, Sandy L. Baccam, Michelle Axford, John D. Cleary, James M. Moore, Bryce L. Sopher, Stephen J. Tapscott,, Galina N. Filippova, Christopher E. Pearson & Albert R. La Spada. PLOS Genetics (November 2008).

Thermoregulatory Defects in Huntington's disease Transgenic Mice Result from PGC-1 alpha Transcription Interference. Patrick Weydt, Victor V. Pineda, Anne E. Torrence, Eduardo R. Lazarowski, Randell T. Libby, Terrence F. Satterfield, Merle L. Gilbert, Gregory J. Morton, Theodor K. Bammler, Andrew D. Strand, Libin Cui, Dimitri Krainc, Richard P. Beyer, Courtney N. Easley, Annette C. Smith, Serge Luquet, Ian R. Sweet, Michael W. Swartz and Albert R. La Spada. Cell (Metabolism) 4:349-362 (2006).

Bergmann Glia Expression of Polyglutamine-Expanded Ataxin-7 produces Purkinje Cell Degeneration and Implicates Glial-Induced Impairment of Glutamate Transport in SCA7. Sara K. Custer, Gwenn A. Garden, Nishi Gill, Randell T. Libby, Stephen J. Guyenet, Lesnick E. Westrum, Bryce L. Sopher and Albert R. La Spada. Nature Neurosciences (Submitted, 2005).

Neuronal Apoptosis Induced by the HIV-GP120* Coat Protein Involves P53 Mediated Down Regulation of XIAP. Christina Tun, Weiqun Guo, Bomy yun, Randell T. Libby, Richard S. Morrison and Gwenn A. Garden. J. Biol. Chem. (Submitted, 2005).

A SCA7 CAG/CTG repeat Expansion is Stable in Drosophilia melanogaster Despite Modulation of Genomic Context and Gene Dosage. Stephen M. Jackson, Alex J. Whitworth, Jessica C. Greene, Randell T. Libby, Sandy L. Baccam, Leo J. Pallanck and Albert R. La Spada. Gene 347:35-41 (2005).

Androgen Receptor YAC Transgenic Mice Recapitulate SBMA Motor Neuronopathy and Implicate VEGF 164 Expression in The Motor Neuron Degeneration. Bryce L. Sopher, Ph.D., Patrick S. Thomas, Michelle A. LaFevre-Bernt, Ph.D., Ida A. Holm, M.D., Scott A. Wilke, Carol B. Ware, Ph.D., Lee-Way Jin, M.D., Randell T. Libby, Ph.D., Lisa M. Ellerby, Ph.D., Albert R. La Spada, M.D., Ph.D. Neuron 41:687-699 (2004).

Genomic Context Drives SCA7 CAG Repeat Instability, while Expressed SCA7 cDNAs are Intergenerationally and Somatically Stable in Transgenic Mice. Randell T. Libby, Darren G. Monckton, Ying-Hui Fu, Refugio A. Martinez, John P. McAbney, R. Lau, David D. Einum, K. Nichol, Carol B. Ware, Louis J. Ptacek, Christopher E. Pearson & Albert R. La Spada. Hum. Mol. Genet. 12:41-50 (2003).

Polyglutamine-Expanded Ataxin-7 Promotes Non-Cell Autonomous Purkinje Cell Degeneration and Displays Proteolytic Cleavage in Ataxic Transgenic Mice. Gwenn. A. Garden, Randell T. Libby, Ying-Hui, Fu, Yoshito. Kinoshita, Jing. Huang, Daniel. E. Possin, Annette. C. Smith, Refugio. A. Martinez, Gabriel. C. Fine, Sara. K. Grote, Carol. B. Ware, David. D. Einum, Richard. S. Morrison, Louis. J. Ptacek, Bryce. L. Sopher and Albert. R. La Spada. J. of Neurosciences 22:4897-4905 (2002).

Polyglutamine-Expanded Ataxin-7 Antagonizes CRX Function and Induces Cone-Rod Dystrophy in a Mouse Model of SCA7. Albert R. LaSpada, Ying-Hui Fu, Bryce L. Sopher, Randell T. Libby, Xuejiao Wang, Lili Y. Li, David D. Einum, Jing Huang, Daniel E. Possin, Annette C. Smith, Refugio A. Martinez, Kari L. Koszdin, Piper M. Treuting, Carol B. Ware, James B. Hurley, Louis J. Ptacek and Shiming Chen. Neuron 31:913-927 (2001).

Molecular Modeling and Preclinical Evaluation of the Humanized NR-LU-13 Antibody. Scott S. Graves, Stephen C. Goshorn, Diane M. Stone, Don B. Axworthy, John N. Reno, Becky Bottino, Stephen Searle, Andrew Henry, Jan Pedersen, Anthony R. Rees and Randell T. Libby. Clinical Cancer Research 5:899-908 (1998).

Phosphorolytic Error Correction During Transcription. Randell T. Libby and Jonathan A. Gallant. Molecular Microbiology 12:121-129, 1994.

The Role of RNA Polymerase in Transcriptional Fidelity. Jonathan A. Gallant and Randell T. Libby. Molecular Microbiology 5:999-1004, 1991.

Transcriptional Proofreading in Escherichia coli. Randell T. Libby, Jeffrey N. Nelson, Joseph M. Calvo, and Jonathan A. Gallant. EMBO 8:3153-3158, 1989.

Flag Peptide: A Short Polypeptide Marker Sequence Useful for Recombinant Protein Expression and Purification. Thomas P. Hopp, Kathryn S. Prickett, Virginia Price, Carl J. march, Randell T. Libby, David L. Urdal, and Paul J. Conlon. BioTechnology 6:1204-1210, 1988.

Human Rhinovirus 3C Protease: Cloning and Expression of an Active Form in Escherichia coli. Randell T. Libby, David Cosman, Carl J. March, and Thomas P. Hopp. Biochemistry 27:6262-6268, 1988.

Structure and Expression of the Gene, mcrBDCGA, which Encode the Subunits of Component C of Methyl Coenzyme M Reductase in Methanococcus vannielii. D. S. Cram, B. A. Sherf, R. T. Libby, R. J. Mattaliano, K. L. Ramachandran and J. N. Reeve. Proc. Natl. Acad. Sci. USA. 84:3992-3996, 1987.

Expression and Purification of Native Human Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) from an Escherichia coli Secretion Vector. Randell T. Libby, Gary Braedt, Teresa A. Chiaverotti, Shirley R. Kronheim, Carl J. March, David L. Urdal, Robert J. Tushinski, and David Cosman. DNA 6:221-229, 1987.

cDNA Cloning, Expression, and Activity of Human Granulocyte-Macrophage Colony Stimulating Factor. Michael A. Cantrell, Dirk Anderson, Virginia Price, Michael Deely, Randell T. Libby, Kenneth H. Grabstein, Douglas Pat Cerretti, Diane Y. Mochizuki, Robert J. Tushinski, and David Cosman. IN: Recombinant Lymphokines and Their Receptors, (ed. S. Gillis), Chapter IX, Marcel Dekker, Inc., New York, NY, 1986.

Mistranslation of the mRNA Encoding Bacteriophage T7 0.3 Protein. Jacqueline B. Rice, Randell T. Libby, and John N. Reeve. J. Biol. Chem. 259:6505-6510, 1984.

Mistranslation in Bacteriophage-Infected Anucleate Minicells of Escherichia coli: A Test for Error Propagation. Randell T. Libby. Mech. Age. Develop. 26:23-28, 1984.

Expression of Coliphage T7 in Aging Anucleate Minicells of Escherichia coli. Randell T. Libby, Jocelyn E. Shaw, and John N. Reeve. Mech. Age. Develop. 27:197-206, 1984.

RNA Polymerase Subunit Biosynthesis in Bacillus subtilis. Randell T. Libby and Lyle R. Brown. Mol. Gen. Genet. 185:339-343, 1982.

Biosynthesis of RNA Polymerase in Bacillus subtilis During Induction of the Stringent Response. Randell T. Libby, Sarah J. Kuhl, and Lyle R. Brown. IN: Sporulation and

Germination, Proceedings of the VIII International Spore Conference, Woods Hole, Massachusetts, pp. 145-149, 1981.

Invited Presentations/Selected Abstracts

Exon Array Analysis Reveals Significant Aberrant Splicing in SALS Motor Neurons. Stuart Rabin, Randell T. Libby, Hugo Kim, Young Kim, Brad Stone, Al LaSpada and John Ravits. American Academy of Neurology (AAN), Seattle, Washington, 2009

CTCF Binding Regulates Ataxin7 Gene Expression: A Novel System for Transcription Control. R. T. Libby, B. L. Sopher, D. Cho, S. Baccam, S. J. Tapscott, G.N. Filippova and A. R. La Spada. American Society of Human Genetics (ASHG), Salt Lake City, Utah, 2005.

Body Temperature Links Metabolism and Transcriptional Dysregulation in a Mouse Model of Huntington's Disease. Patrick Weydt, Victor Pineda, Randell T. Libby, Annette C. Smith, Jenny Choi, Philamer Calses, Courtney Easley, Serge Luquest and Albert R. La Spada. Gordon Research Conference on CAG Triplet Repeat Disorders, Mount Holyoke College, Hadley, Massachusetts, 2005.

Body Temperature Links Metabolism and Transcriptional Dysregulation in a Mouse Model of Huntington's Disease. Patrick Wyedht, Victor Pineda, Randell T. Libby, Annette C. Smith, Jenny Choi, Philamer Calses, Courtney Easley, Serge Luquest and Albert R. La Spada. II. Meeting on the Molecular Mechanisms of Neurodegeneration. Milan, Italy 2005.

Glial Expression of PolyQ Ataxin-7 is Sufficient to Cause Purkinje Cell Degeneration: A Model of Non-Cell Autonomous Cerebellar Ataxia. Society for NeuroSciences, San Diego, 2004.

Microarray Expression analysis of a YAC Transgenic Mouse Model of Spinal & Bulbar Muscular Atrophy: Is Transcription Dysregulation Important for Androgen Receptor Polyglutamine Neurotoxicity? R. T. Libby, L. Chakrabarti, A. C. Smith, and A. R. La Spada. Society for Neurosciences, 5th Brain Research Symposium, New Orleans, 2003.

HIV/gp120 Induced Neuronal Apoptosis Involves p53 Mediated Trans-Repression of XIAP . C. Tun, W. Guo, R. Libby, R.S. Morrrison, G.A. Garden. Society for Neurosciences, New Orleans, 2003

SCA7 Locus Information Drives Trinucleotide Repeat Instability in Transgenic Mice. R. T. Libby, R. Lau, D. D. Einum, K. Nichols, L. J. Ptacek, Y. H. Fu, C. E. Pearson and A. R. LaSpada. American Society of Human Genetics, San Diego (October 2001).

Polyglutamine-Expanded Ataxin-7 Induces a Cone-Rod dystrophy in Transgenic Mice by Antagonizing the Function of the Nuclear Transcription Factor CRX. A. R. LaSpada, Y.-H. Fu, B. L. Sopher, R. T. Libby, X. Wang, L. Y. Li, D. D. Einum, J. Huang, D. E. Possin, J. B. Hurley, L. J. Ptacek, and S. Chen. American Society of Human Genetics, San Diego (October 2001).

Neurological Dysfunction in a Mouse Model of SCA7 is Associated with Proteolytic Cleavage og Polyglutamine-Expanded Ataxin-7. Bryce L. Sopher, Ying-Hui Fu, Randell T. Libby, Yoshita Kinoshits, David D. Einum, ing Huang, Daniel E. Possin, Richard S. Morrison, Louis J. Ptacek and Albert R. LaSpada. American Society of Human Genetics, San Diego (October 2001).

SCA7 Transgenic Mice Show a Cone-Rod Dystrophy Type of Retinal Degeneration and a Neurological Phenotype. A. R. LaSpada, B. L. Sopher, R. T. Libby, D. D. Einum, J. B. Hurley, J. Huang, D. E. Possin, L. J. Ptacek and Y. –H. Fu. Keystone Symposia: The Molecular Basis of Neurodegenerative Disease. 2001.

Microfectin™ Gene Delivery Technology: Novel Non-Ionic Emulsion-Based Nucleic Acid Delivery Systems. Christopher W. McDaniel, Lawrence L. Kunz and Randell T. Libby, AAPS Abstract, 1999.

Cytoskeletal Functions and Their Role in Restenosis: Inhibition of Chronic Vascular Remodeling by Cytochalasin B. Lawrence L. Kunz, Lauren M. Tatalick, Debora A. Libby, Randell T. Libby, Nicholas P. Ranieri, Robert W. Schroff. Restenosis Summit VII, Cleveland (May, 1995).

U.C.L.A. Arrowhead Genetics Conference, The Secret Life of RNA Polymerase (Abstract), 1989.

Purification and Reconstitution of the Methyl Reductase Enzyme from Methanococcus vannielii.. Randell T. Libby. American Society for Microbiology, 1984.

In-vivo and In-vitro Transcription Map of the *Bacillus subtilis* Bacteriophage, TSP-1. Sarah J. Kuhl, Randell T. Libby, and Lyle R. Brown. American Society for Microbiology, 1981.

The RNA Polymerase of *Bacillus subtilis*: Regulation, Assembly, and Relative Rates of Subunit Biosynthesis. Randell T. Libby, Ph.D. Thesis, Oregon State University, Corvallis, 1980.

Conferences/Invited Lectures/Additional Training (Selected List)

20th International Symposium on Human Identification, Las Vegas, Nevada, 2009

Agilent/Science, Noncoding RNAs: A Paradigm for Gene Regulation, Webinar, 2008

Applied Biosystems, GeneMapper-X, Webinar Training, 2008

XVth International Symposium on Human Identification, Phoenix, Arizona, 2004

4th International Conference on Unstable DNA Elements, Banff, British Columbia, 2004.

52nd Annual American Academy of Forensic Sciences Meeting, Reno, Nevada, 2000.

Perkin Elmer Gene Discovery A Systems Approach to Linkage Mapping, Seattle, Washington (1999).

Perkin Elmer ABI 310, ABI 377, ABI 3700 Sequencing Users' Meeting, Seattle, Washington (1999).

2nd International Conferences on Unstable DNA Elements, University of North Carolina, Chapel Hill, NC, 1999

University of Washington, Short Tandem Repeats (STRs) in Forensic DNA Genotyping, Invited Lecturer, 1999.

Perkin Elmer GeneScan User's Meeting, Seattle, Washington (1998).

VIIIth International Symposium on Human Identification (Participant), Scottsdale, Arizona, 1997.

1st International Conference on Gene Therapy: Delivery and Quantitation. (Participant), La Jolla, California, (1997).

IInd International Conference on Advances in the Effective Delivery of Proteins, Peptides and Nucleic Acids. Coronado, California, 1996. (Invited Participant).

Jacques Monod Conference: Morphogenic Functions of Actin-Associated Proteins, Centre National De La Recherche Scientifique (CNRS), Aussois, France, 1995 (Invited Participant).

Perkin Elmer Conference: Accelerating Gene Discovery & Mutation Detection - Breakthroughs In Human Genetics & Disease Research, Seattle, Washington, 1995.

VIth International Symposium on Human Identification (Participant), Scottsdale, Arizona, 1995.

International Symposium on Cellular and Molecular Biology of Phosphate and Phosphorylated Compounds in Microorganisms (Invited Participant), Phosphorolytic Error Correction During Transcription, Woods Hole, MASS, 1993.

IVth International Symposium on Human Identification, Scottsdale, Arizona, 1993.

IIIrd International Symposium on Human Identification, Scottsdale, Arizona, 1992.

Centre National de la Rescherche Scientific (CNRS), Jacques Monod Conference, Invited Participant, Roscoff, France, 1990.

Universite de Paris VII, International Congress of RNA Polymerases, Keynote Speaker, 1989.

University of Hawaii, Maintenance of Transcriptional Fidelity in *Escherichia coli*, Invited Speaker, 1989.

U.C.L.A. Arrowhead Genetics Conference, Transcriptional Error Monitoring in *Escherichia coli*, Invited Speaker, 1989.

U.C.L.A. Arrowhead Genetics Conference, The Secret Life of RNA Polymerase (Abstract), 1989.

XVIth International Congress of Genetics, Transcriptional Regulation in *Escherichia coli* (Abstract), Toronto, Canada, 1988.

Gordon Conference (Population Biology and Evolution of Microbiology), A Novel Immunological Method for the Characterization of rDNA Molecules (Abstract), Plymouth, New Hampshire, 1987.

NeoRx Corporation, Cloning and Expression of the Human Lymphokines IL-1 and GM-CSF. Invited Speaker, 1987.

California Institute of Technology, Beginning Genetics of Methanogenic Organisms, Invited Speaker, 1983.

Texas Tech University, Protein Instability in Anucleate Minicells of *Escherichia coli*. Invited Speaker, 1982.

European Molecular Biology Organization (EMBO): Workshop on Accuracy (III), Error Propagation in Bacteriophage-Infected Anucleate Minicells of *Escherichia coli*. Grignon, France. Invited Speaker, 1983.

European Molecular Biology Organization (EMBO): Workshop on Accuracy (II), Catalytic Error Damping Systems in *Escherichia coli*. Grignon, France. Invited Speaker, 1981.