Curriculum Vitae DAVID JOHN GALAS

PERSONAL

<u>Citizenship</u> : Marital Status:	February 25, 1944 (St. Petersburg, FL) – May 27, 2023 (Bainbridge Island, WA) USA Married to Diane R. Isonaka; two adult children
ADDRESSES	
<u>Business</u> :	Pacific Northwest Research Institute 720 Broadway Seattle, WA 98122 Phone: 206 568-1487 dgalas@pnri.org
<u>Home</u> :	111 W. Comstock Street Seattle, WA 98119 Phone: 206 285-0521
EDUCATION	
1972	University of California, Davis-Livermore, Physics: Ph.D. Dissertation: "Theory of Interaction of Impurities with Liquid Helium"
1968	University of California, Davis-Livermore, Physics, M.S.
1967	University of California, Berkeley, Physics, A.B. with honors
<u>Other</u>	
1974	Cold Spring Harbor Laboratory Summer study in the Molecular Biology & Genetics of Yeast
1975	Cold Spring Harbor Laboratory Summer study in Advanced Molecular Genetics of Bacteria
PROFESSIONAL H	ISTORY
2012 – Present	Principal Scientist Pacific Northwest Research Institute, Seattle, WA
2008 – 2012	Senior Vice President for Strategic Partnerships Institute for Systems Biology, Seattle, WA
2005 – 2012	Professor, Institute for Systems Biology
2005 – 2008	Vice President, Chief Science Officer for Biology and Life Sciences Battelle Memorial Institutes
2002 – 2005	Chancellor, Chief Scientific Officer and Norris Professor of Applied Life Sciences Keck Graduate Institute of Applied Life Sciences, Claremont, CA
1998 – 2002	Chief Academic Officer, Dean of Faculty, Vice President, Norris Professor of Applied Life Sciences, Keck Graduate Institute of Applied Life Sciences
1997 - 1998	President and Chief Scientific Officer, Director Chiroscience R&D Inc. (formerly Darwin Molecular Corporation)

1995 - 1997	Executive Vice President and Chief Scientific Officer, Director Darwin Molecular Corporation
1994 - 1996	President, CEO and Chief Scientific Officer Darwin Molecular Corporation
1993 - 1994	Vice President for Research and Development, Founder & Director Darwin Molecular Corporation
1990 - 1993	Director for Biological and Environmental Research, Office of Energy Research, U.S. Department of Energy (on leave from the University of Southern California)
1988 - 1993	Professor of Molecular Biology, Department of Biological Sciences University of Southern California
1985 - 1990	Chairman of Molecular Biology, University of Southern California
1984 - 1988	Associate Professor (with tenure), Molecular Biology, Department of Biological Sciences, University of Southern California
1981 - 1984	Assistant Professor, Molecular Biology, Department of Biological Sciences University of Southern California
1977 - 1981	Charge' de Recherches, Department of Molecular Biology, University of Geneva, Geneva, Switzerland
1974 - 1977	Senior Staff Scientist, Biomedical Division, University of California Lawrence Livermore National Laboratory, Livermore, California
1972 - 1974	Scientific Advisor to Defense Science Board, Task Force on Strategic Vulnerability (Capt., USAF)
1967 - 1972	Hertz Foundation predoctoral fellow
1966 - 1967	Computational Technician/Programmer, Theoretical Physics Department University of California, Lawrence Livermore National Laboratory

OTHER ACADEMIC APPOINTMENTS

Visiting Professor, Luxembourg Centre for Systems Biomedicine, University of Luxembourg, 2009-present

Adjunct Professor, Department of Bioengineering, University of California San Diego, La Jolla, CA 2000 - 2007

Adjunct Professor, Department of Molecular Virology, Immunology and Medical Genetics, Ohio State University Medical School, Columbus, Ohio 2005 - 2008

BOARDS/COMMITTEES

Editorial Boards

Editorial Board, exRNA, 2021 - present Editorial Board, Journal of Bioinformatics and Computational Biology, 2002 - present Editorial Board, Functional & Integrative Genomics, 1999 – present Editorial Board, Journal of Computational Biology, 1993 – present Editorial Board, Current Proteomics, 2003 – present Editorial Board, Medical Bioinformatics, 2008 - present Editorial Board, Journal of Clinical Bioinformatics, 2009 – present *CV - David J. Galas* Editorial Board, Entropy, 2020 - present

National Academy of Sciences – National Research Council

National Academy of Sciences, Board on Biology, 1995-2000

National Academy of Sciences, Commission on Life Sciences, 1998-2000

National Academy of Sciences, Board on Life Sciences, 2000 - 2003

National Research Council Panel on "The Scientific and Medical Aspects of Human Cloning," 2001

National Research Council Steering Committee Member on "Defining the Mandate of Proteomics in the Post-Genomics Era," 2002

The National Research Council, Biological Panel, Committee on "Science and Technology for Countering Terrorism", 2002

The National Research Council, Committee on "The Future of Proteomics", 2003

National Academy of Sciences, Panel on Science, "Technology and Law," 2003-2007

National Academy of Sciences, Committee on "Emerging Issues and Data on Environmental Contaminants," 2006-2007

National Academy of Sciences, Chair of Committee on "Defining and Advancing the Conceptual Basis of Biological Sciences in the 21st Century," 2007-2008

National Academy of Sciences, Engineering, and Medicine – Health & Medicine Division Committee, 2015 - 2020

Academic

Advisory Board, Boston University Bioinformatics Program, 1999 – 2005

Scientific Advisory Board of the Institute for Molecular Bioscience, The University of Queensland, Australia, 2003 - 2008

Bioinformatics Institute Review Committee, A-star, Biopolis Singapore, 2008-2009

Genomics Institute Review Committee, A-star, Biopolis Singapore, 2009 Advisor to Luxembourg Centre for Systems Biomedicine, University of Luxembourg 2008 -present Scientific advisory Committee, University of Utah Department of Human Genetics, 1995-2000

Non-profit

Scientific Advisory Board, NOVIM, 2017 - present

Chairman Emeritus, Fannie and John Hertz Foundation, 2022

Chairman of the Board of Directors, Fannie and John Hertz Foundation, 2008 – 2022

Board of Directors, Fannie and John Hertz Foundation, 1999 - present

Selection Committee for the Howard Hughes Medical Institutes Investigators in Computational Biology, 1999 – 2001

Board of Governors, National Center for Genome Resources, Santa Fe, New Mexico, 1995 - 2000

Board of Directors, Washington Research Foundation, Seattle, Washington 2010-present

Companies

Board of Directors, Impath Inc., 1999 – 2002 (public corporation, US NASDAQ) Board of Directors, Rapigene Inc., 1998 – 1999 (spin-out of Chiroscience plc) Board of Directors, Chiroscience Group plc, 1997 - 1998 (public corporation, London Stock Exchange) Board of Directors, Blue Heron Technologies Inc. (private biotechnology company), 1999 – 2007 Chairman of the Board, Ionian Technologies Inc. (private biotechnology company), 2002 – 2010 Board of Directors, NATDx Inc. (private biotechnology company), 2015-present Scientific Advisory Board, Blue Heron Technologies, 2000 - 2010 Scientific Advisory Council, CellTech Group plc, (public corporation, London Stock Exchange) 1999 – 2003 Scientific Advisory Board, Impath Inc., 1999 - 2002 Business and Scientific Advisory Board, Axiom Venture Partners, 2003 – 2009 Scientific Advisory Board, Integra Ventures, 2001- 2008 Scientific Advisory Board, Valigen Corp., Paris, 2000 - 2002 Scientific Advisory Board, Cyvera, 2004 – 2005 Scientific Advisory Board, Integrated Diagnostics Inc., (private biotechnology company) 2009 – 2012 Scientific Advisory Committee, Regeneron, 2011

Government, National Laboratory

NCI/ DOE Collaborations Working Group, 2018 - present Policy Board, DOE Joint Genome Institute, University of California, 2000 - present Advisory Committee, DOE Joint Genome Institute, University of California, 1997 – 2000 Advanced Scientific Computing Advisory Committee, DOE, Washington, DC, 2003 - 2009 National Biotechnology Policy Board, 1990 - 1993 National Cancer Advisory Board, 1990 - 1993 Vice Chairman, Committee on Life Sciences and Health, Federal Coordinating Committee for Science Education and Technology (OSTP), 1990 - 1993 Chair, Biotechnology Research Subcommittee, Committee on Life Sciences and Health, (OSTP), 1990 – 1993 Committee on Earth and Environmental Science, Federal Coordinating Committee for Science Education and Technology, (OSTP), 1991 – 1993 Chair, Biology Division Review Committee, Los Alamos National Laboratory, 2000 - 2007 Laboratory Advisory Committee, Pacific Northwest National Laboratory, 2001 - 2005 Biological System Institute Advisory Committee, Pacific Northwest National Laboratory, 2001-2000 Director's Advisory Committee, Pacific Northwest National Laboratory, 2001-2005 NIH Director's Advisory Committee on "High Risk Research Initiatives", 2003 Science and Technology Steering Committee, Brookhaven National Laboratory, 2005 – present NCI-DOE Cancer Advisory Committee, 2005 – 2007 NIH Director's Advisory and Selection Committee, "Director's Pioneer Awards", 2004, 2005, 2006, 2008, 2019

HONORS

A.B. with Honors in general scholarship and Physics, UC Berkeley, 1967

Rhodes Scholarship finalist, 1967

Fannie and John Hertz Foundation predoctoral fellowship, 1968 - 1972

NSF predoctoral fellowship, AEC predoctoral fellowship (declined), 1968

My first biology paper recognized as: "Benchmark Papers in Genetics", 1976 (see Publications)

Friedrich-Miescher Award in Biochemistry, nominee for DNA "footprinting," Swiss Biochemical Society, 1981

Parker Award and Lecturer, Battelle-Pacific Northwest Laboratories, 1995

Co-founder, Darwin Molecular Corporation

Founder, Rapigene

Founder, Ionian Technologies Inc.

Founder, Zuyder Inc.

Co-founder, Integrated Diagnostics

Smithsonian Institution – Computerworld Pioneer Medal (for role in International Human Genome Project), 1999

Co-founder, Keck Graduate Institute, 7th Claremont College, 1999

Endowed chair: Kenneth T. and Eileen L. Norris Professor of Applied Life Sciences, Keck Graduate Institute, 2000 – 2005

Lifetime National Associate of the National Academy of Sciences, 2003

Co-organizer of the 1st through the 10th Aegean conference on "Pathways, Networks and Systems, Theory and Experiments" 2003 - 2012

Membership and chairmanship of many NAS/NRC committees Appointed to the Council on Healthcare of the World Economic Forum, 2011

SOCIETIES

American Physical Society American Chemical Society American Society of Human Genetics American Association for the Advancement of Science American Society of Microbiology Human Genome Organization Sigma Xi Genetics Society of America New York Academy of Sciences

SUMMARY OF SCIENTIFIC INTERESTS

My scientific interests are multiple and include the integration and application of a variety of disciplines to solving biological and medical problems. This includes, particularly, mathematical and computational methods, but also the application of physical methods in the development of novel approaches to the analysis of biological systems at the molecular level. These particular applied interests are evident in my role in co-founding and managing biotechnology companies, Darwin Molecular Corporation (DMC) in particular. DMC was founded in 1993 to take advantage of new developments in gene discovery and combinatorial chemistry to forge a gene-to-drug discovery capability within a small company. These ambitions were large, but the work included the discovery of the Werner's Syndrome gene (the first human gene found to directly affect aging), and a gene for susceptibility to early onset Alzheimer's disease, a novel human gene involved in the control of bone density, and the development of several novel technologies for rapid genotyping, gene expression profiling, and several other genomic analysis methods. The later resulted in the founding of another new company in 1998, Rapigene Inc. The bone gene, SOST, encodes an osteocyte protein whose inhibition reliably increases bone mineral density. An inhibiting antibody is in phase three trials. I recently founded a company, Ionian Technologies Inc., based on technology from my laboratory at the Keck Graduate Institute. The various technological advances in methods for the amplification and measurement of nucleic acids as diagnostics is contributing significantly to bringing the benefits of the life sciences to society in molecular analysis of disease correlates and developing world diagnostics. Ionian was acquired by Alere in 2010.

The development of new technologies and diverse methods that can be used to characterize biological systems and their function is essential for the development of the new science of biology that involves the quantitative understanding of complex biological systems. The conceptual convergence of these different disciplinary approaches

is now recognized as the basis of what we now call systems biology. The specific area of understanding the mathematical nature of complex biological systems is of deep interest to me. I believe the information-complexity approach is the most promising of these approaches, but it is clear that biology will be a rich source of mathematical problems, and mathematics will be increasingly important to the understanding of biology. Most recently I have been working on approaches to integrate genetics with systems biology by developing new methods for analyzing genetic (and other data), notably using recent AI approaches that employ probabilistic logic methods, and a new information theory-based approach that appears to be very general and effective.

Policy interests that I have pursued in my governmental work include the nature of the effects of technological developments on the advance of biological research and applications in public and private sectors, and the interactions of these sectors. My involvement in the leadership of the Human Genome Program (the DOE component of the project was my responsibility from 1990 to 1993) has sharpened those interests and convinced me of the major role to be played by technology in the future of all the basic and applied life sciences. Both anticipation of scientific advances and the formulation of effective policy for research are strongly affected by this connection. My involvement in directing and coordinating the FY 1993, multi-agency, Presidential Initiative in Biotechnology Research (see the 1993 Presidential Report Entitled, "Biotechnology For the 21st Century" and the follow-on document for 1994) has given me a deep appreciation of the fundamental nature of basic-applied-technology feedback loops that operate over a wide range of modern scientific research activities, and the way that research is handled in government. Other policy-related research interests include those related to gene patents, radiation effects, mutagenesis and carcinogenesis, and in particular the effects of specific genotypes on the biological manifestation of DNA damage, and other pathogenic processes. I served on the National Academy Panel on Science Technology and Law that explored some of these important policy issues.

Another major active interest is in the understanding of the roles of non-coding RNAs in biology, including regulatory roles, as biomarkers and for intercellular communication. This is a very active topic in my laboratory and has recently resulted in strong evidence that RNA molecules from the microbiome of humans and mice enter the blood plasma in some way. The possibility that the composition and activity of the microbiome is reflected in plasma RNA markers, or that there is an actual function effect of these exogenous RNA is being explored.

Significant Research Discoveries/Accomplishments in Biology

- 1. Evidence for potential informational instability in biological processes protein synthesis errors in *E. coli* can feedback, become progressive and unstable (1975) [paper reprinted in <u>Benchmark Papers in Genetics Series</u>]
- 2. An inverse relationship between ribosome speed and fidelity of protein synthesis discovered using *E. coli* ribosomal mutants defined kinetic parameters of accuracy in the translation of the genetic code (1976)
- 3. The "footprinting" method for defining the exact position of DNA-binding proteins on their binding sites. This is the first and still most widely used method for defining protein binding sites on the DNA (1978)
- 4. A bacterial protein can severely bend DNA at specific sites the most serve such effect observed. The IHF protein bends DNA approximately 120° (bending discovered at both ends of the transposable insertion sequence IS<u>1</u>) (1984)
- 5. The transposition rate of IS<u>1</u> is regulated by *translational frameshifting* on the mRNA transcript fused transposase protein competes with unfused repressor. This discovery defined a novel regulatory mechanism, seen previously in retroviruses, for regulating the movement of bacterial transposable genetic elements (1987)
- Human gene discovery: Susceptibility to early onset Alzheimer's disease can be caused by missense mutations in a membrane protein gene (presenilin 2 - PS2). The mutant protein mis-processes amyloid protein as well as others. This protein is now recognized as one of two gamma-secretase enzymes involved in amyloid protein processing (1995)

- 7. Human gene discovery: First identified human gene that affects the rate of aging was discovered. The Werner's Syndrome gene is a DNA helicase. Conceived of and led a collaborative project team that found the gene by positional cloning (1996)
- Discovery of a gene in both mice and men that when mutated leads to a serious lymphoproliferative disorder

 the FoxP3 gene. Causes severe hyper-inflammatory response of the immune system. X-linked mutation is
 fatal in infancy in males. This protein we called *scurfin* is encoded by FoxP-3. It is a key transcription factor in
 the development and stability of regulatory T-cells (1997)
- 9. Human gene discovery: New human gene regulating bone mineral density called SOST. The recessive genetic disorder, sclerosteosis is caused by loss of gene function in a gene encoding a cystine-knot protein called sclerostin. Identified a new pathway for regulation of bone mineral metabolism (involving the Wnt pathway) that is now known as a promising area for therapeutic discovery for osteoporosis (1999)
- 10. Discovered a new class of isothermal nucleic acid amplification reactions and invented several schemes for developing diagnostic tools using them. The biotech company, Ionian Technologies Inc. was founded based on this discovery/invention (2002)

GOVERNMENT AND INDUSTRY EXPERIENCE

My experience in government service as Director of Health and Environmental Research in the Department of Energy, Office of Science, from 1990 to 1993 involved running all the programs of research in biological and environmental sciences. This research was carried out in the National laboratories and in Universities across the country, and covered a wide range of areas in basic and applied science and technology, including most notably the component of the Human Genome Project of the Department of Energy, a project that I participated in initiating. The DOE component was approximately one half the size of the NIH program during that time. The government rank of my position was at the level of a Deputy Assistant Secretary. The research budget managed at the end of this time was approximately \$480MM. My objectives in this job were to maximize the effectiveness and scientific strength of the Human Genome Program, re-invigorate the DOE programs with research that takes full advantage of new molecular and computational technologies, the technologies of the national laboratories, and to integrate and realign existing programs in both the national labs and universities with these goals. I was substantially successful in setting these programs on the path to meeting these objectives (see for example Galas and Collins, paper on the five-year plan for the Human Genome Project in Science, 1993).

In the private sector, I was one of the founders in 1993 of Darwin Molecular Corporation, a biotechnology company focused on an integrated technological approach to drug discovery that began with gene discovery and used combinatorial chemistry methods to developed drug leads against newly defined targets. This plan for a small company was considered heretical at the time, but has since become commonplace in the industry. I was the chief scientific officer from the company's inception and have also held other positions as needed, including CEO, and most recently President of the US component of the larger merged company when it was acquired by a public British company. We were successful in discovering several significant new genes including the gene for Werner's syndrome, the first human gene known to directly affect aging, an Alzheimer's disease susceptibility gene, PS2, a new human bone density gene, and several others that are now making contributions to the current company pipeline. The one gene, in particular, has a good chance of contributing to the effective treatment of osteoporosis (Amgen-UCB). The company merged in January 1997 with a UK company, Chiroscience plc, which was focused on chemistry, and preclinical and clinical drug development. I remained the President and Chief Scientific Officer of the US part of the combined company until my resignation in 1998 to assume the role at KGI. With some new technology developed in Darwin Molecular at the foundation, we formed a new subsidiary, Rapigene, in March 1998 to develop and commercialize this genotyping and gene expression measurement technology. This spin-off was acquired by Qiagen. Chiroscience plc was acquired by Celltech in 1999, and Celltech was later acquired by the Belgian pharma company, UCB.

In September 1998 I relinquished all management responsibilities for Chiroscience and assumed a part time advisory role in order to assume the post of Chief Academic Officer and to help found a new academic venture, the Keck Graduate Institute of Applied Life Sciences (KGI). KGI was formed to develop an entirely new type of graduate training and research program focused primarily on training professionals in the applied life sciences. Integrating a range of technical and management components, KGI will train leaders for the future of the biotechnology, health care and pharmaceutical industry, and carry out focused research on a variety of applied problems in the life sciences. One designated area of focus is on the applications of computational and theoretical methods to applied problems in the life sciences. The institute is the newest chartered member of the Claremont College consortium and has the potential to contribute to significant change in training in the life sciences, particularly for applications and at the interface of science, technology and business. While at KGI two companies were formed around technology originating in my research laboratory. One of these, Ionian Technologies was acquired by Alere in 2010.

In June 2005 I assumed the position of Vice President and Chief Science Officer for Biology and Life Sciences at Battelle Memorial Institute. I also took an academic position as Professor at the Institute for Systems Biology, a non-profit research institute in Seattle, WA. My responsibilities in the newly created Battelle position were to plan and coordinate Battelle's various activities in the life sciences – in the national labs managed by Battelle, and in the other commercial and government contract work that Battelle performs. Battelle allowed me time to attend to my own research and policy interests. The major accomplishment at Battelle was to start a coordinated research effort, including academic and national lab investigators focused on pulmonary disease, which has produced some exciting and useful results. I assumed the position of Senior Vice President of the Institute for Systems Biology in 2008, focused on devising and managing new strategic partnerships with the Institute, like the recent research and collaboration with the country of Luxembourg (approximately \$100MM research effort in the US and Luxembourg over 5 years.) As the principal investigator of the program, my research is supported by this Luxembourg program. This funding and the relationship of my laboratory with the University of Luxembourg continues following my departure from ISB to join the Pacific Northwest Diabetes Research Institute in September 2013.

Significant Non-Research, Administrative & Entrepreneurial Accomplishments

- 1. Chairman of Molecular Biology, University of Southern California, 1985 1990
- 2. Discussions, organization and lobbying in the scientific community that led to starting the Human Genome Project (HGP) 1986 1990. Several instances of giving testimony before congressional committees related to this effort
- Directed the Office of Biological and Environmental Research in the Department of Energy, including the DOE component of the Human Genome Project, 1990 1993 (Acquired, administered and defended to OMB a ~\$500MM research budget)
- 4. Co-founded several successful biotech companies: including Darwin Molecular Corp., Rapigene Inc., Ionian Technologies Inc, and Integrated Diagnostics.
- 5. Board member of several companies, including: Darwin Molecular Corp., Rapigene Inc., Impath Inc., Blue Heron Biotechnologies, on the Scientific Advisory Board of several other companies, both start-ups and public companies
- 6. President and CEO of Darwin Molecular Corp (1993 1998)
- 7. Chief Scientific Officer of Darwin Molecular Corp (1993 1998)
- 8. Chairman of the Board, Ionian Technologies Inc (2002 2010)
- Chaired a NAS Committee on the Role of Theory in Biology in the 21st Century: report published as a NAS book in 2008
- 10. Created and managed a novel strategic partnership between the Institute for Systems Biology and the Grand Duchy of Luxembourg to build a center for systems biomedicine (five-year budget of ~\$100MM) (2008)
- 11. Introduced Geisinger Healthcare System and Regeneron, and helped catalyze a patient sequencing project relationship, worth about \$100MM, that has been very successful and continues to this day.

PUBLICATIONS

- 1. Galas, D.J., "Galilean Covariance of Gauge Fields and the Quantization of Circulation in He II," <u>Lettre Al</u> <u>Nuovo Cimento</u>, 2:217-221 (1971).
- 2. Galas, D.J., "Theory of the Interaction of Impurities with Superfluid Helium," PhD Dissertation submitted to the University of California (1972).
- 3. Galas, D.J., Jensen, C. A. and Sahlin, H. L., "A Computable Expansion for Multi-particle Propagators," <u>J Math</u> <u>Phys</u>, 14:524-530 (1973).
- 4. Galas, D.J., "The Superleak as a Gyroscope," J Appl Phys, 44:2355-2360 (1973).
- 5. Branscomb, E. W. and Galas, D.J., "Progressive Decrease in Protein Synthesis Accuracy Induced by Streptomycin in *E. coli*," <u>Nature</u> 254:161-163 (1975). (reprinted in <u>Benchmark Papers in Genetics Series,</u> <u>Genes, Proteins and Cellular Aging</u>, ed. R. Holliday, van Nostrand Reinhold Co., New York, (1976).
- 6. Galas, D.J. and Branscomb, E. W., "Ribosome Slowed by Mutation to Streptomycin Resistance," <u>Nature</u> 262:617-619 (1976).
- 7. Galas, D.J. and Branscomb, E. W., "Enzymatic Determinants of DNA Polymerase Accuracy: Theory of T4 Polymerase Mechanisms," J Mol Biol, 124:653-687 (1978).
- 8. Calos, M. P., Galas, D.J. and Miller, J. H., "Genetic Studies of the *lac* Repressor, VIII. DNA Sequence Change Resulting from an Intragenic Duplication," J Mol Biol, 126:865-869 (1978).
- 9. Galas, D.J., "An Analysis of Sequence Repeats in the *lacl* Gene of *E. coli,*" J Mol Biol, 126:858-863 (1978).
- 10. Galas, D.J., "On the Symmetries of Multipalindromic DNA Sequences," J Theor Biol, 72:57-73 (1978).
- 11. Galas, D.J. and Schmitz, A., "DNAase Footprinting: A Simple Method for the Detection of Protein-DNA Binding Specificity," <u>Nucl Acids Res</u>, 5:3157-3170 (1978).
- Clayton, L.K., Goodman, M.F., Branscomb, E.W. and Galas, D.J., "Error Induction and Correction by Mutant and Wild-Type T4 DNA Polymerases: Kinetic Error Discrimination Mechanisms," J Biol Chem, 254:1902-1912 (1979).
- 13. Schmitz, A. and Galas, D.J., "The Interaction of RNA Polymerase and *lac* Repressor with the *lac* Control Region," <u>Nucl Acids Res</u>, 6:111-137 (1979).
- 14. Miller, J.H., Coulondre, C., Schmeissner, U., Schmitz, A. and Galas, D.J., "Altered *lac* Repressors Generated by the Suppression of Nonsense Mutations," in <u>Nonsense Mutations and tRNA Suppressors (pp127-132)</u>, (eds. J.E., Celis and J.D. Smith), Academic Press, London (1979).
- 15. Schmitz, A. and Galas, D.J., "Sequence-Specific Interaction of the Tight-Binding 112-X86 *lac* Repressor with Non-operator DNA," <u>Nucl Acids Res</u>, 8:487-506 (1980).
- 16. Galas, D.J., "Translation and Replication Accuracy: Some Theoretical Considerations", Proceedings of the Conference on Structural Pathology of DNA and the Biology of Ageing, Deutsche Forschungsgemeinschaft, the Zentrallaboratorium für Mutagenitätsprüfung, Freiburg im Breisgau, BRD," <u>Harold Boldt Verlag</u>, Bonn, 108 (1980).

- 17. Miller, J.H., Calos, M.P., Galas, D.J., Büchel, D. and Müller-Hill, B., "Genetic Analysis of Transposition into the *lac* Region of *E. coli*," J Mol Biol, 144:1-18 (1980).
- 18. Galas, D.J., Calos, M.P. and Miller, J.H., "DNA Sequence Analysis of Tn*9* Insertions in the *lacZ* Gene," <u>J Mol</u> <u>Biol</u>, 144:19-41 (1980).
- 19. Galas, D.J., Miller, J.H., Calos, M.P., "Genetic and Sequencing Studies of the Specificity of Transposition into the *lac* region of *E. coli*," <u>Cold Spring Harb Symp Quant Biol</u>, 45:243-257 (1981).
- 20. Galas, D.J. and Chandler, M., "On the Molecular Mechanisms of Transposition," <u>PNAS</u>, 78(8):4858-4862 (1981).
- 21. Chandler, M., Clerget, M. and Galas, D.J., "The Transposition Frequency of IS1-flanked Transposons is a Function of Their Size," J Mol Biol, 154:229-243 (1982).
- 22. Galas, D.J. and Chandler, M., "The Structure and Stability of Tn<u>9</u>-Mediated Cointegrates-Evidence for two Pathways of Transposition," <u>J Mol Biol</u>, 154:245-272 (1982).
- 23. Schmitz, A. and Galas, D.J., "The Study of Protein-DNA Binding Specificity: DNase Footprinting," (review) in <u>Methods in DNA and RNA Sequencing</u>, ed. S. Weissmann, 76 (1984).
- 24. Hirschel, B.H., Galas, D.J. and Chandler, M., "Cointegrate Formation by Tn<u>5</u>, but not Transposition, is Dependent on *recA*," <u>PNAS</u>, 79:4530-4534 (1982).
- 25. Hirschel, B.H., Galas, D.J., Berg, D. and Chandler, M., "Structure and Stability of Transposon-5-Mediated Cointegrates," J Mol Biol, 159:557 (1982).
- 26. Chandler, M. and Galas, D.J., "IS<u>1</u>-mediated DNA Tandem Duplication of Plasmid pBR322: Dependence on *recA*, and on DNA Polymerase I," <u>J Mol Biol</u>, 165:183-190 (1983).
- 27. Chandler, M. and Galas, D., "Cointegrate Formation Mediated by Tn<u>9</u>. II. Activity of IS<u>1</u> is Modulated by DNA Sequences," J Mol Biol, 170:61-91 (1983).
- 28. Galas, D. and Smith, T.F., "The Relationship Between Codon Boundaries and Multiple Reading Frame Preferences: Coding Organization of Bacterial Insertion Sequences," <u>Mol Biol Evol</u>, 1(3):260-268 (1984).
- 29. Waterman, M., Arratia, R. and Galas, D., "Pattern Recognition in Several Sequences: Consensus and Alignment," <u>Bull Math Biol</u>, 46(4):515-527 (1984).
- 30. Chandler, M. and Galas, D., "Studies on the Transposition of IS1," <u>Basic Life Sci</u>, 30:53-77 (1985).
- 31. Galas, D., Eggert, M. and Waterman, M., "Rigorous Pattern Recognition Methods for DNA Sequences: Analysis of Promoter Sequences for *E. coli*," J Mol Biol, 186:117-128 (1985).
- Galas, D., "An Introduction to the Problem of Accuracy," (review) Chapter in <u>Accuracy in Molecular</u> <u>Processes: Its Control and Relevance to Living Systems</u>, Chapman & Hall, London, New York, ed. Kirkwood Rosenberger & Galas (1986).
- 33. Zerbib, D., Gamas, P., Chandler, M., Prentki, P., Bass, S. and Galas, D., "Specificity of Insertion of IS1," <u>J Mol</u> <u>Biol</u>, 185(3):517-524 (1985).

- 34. Gamas, P., Galas, D. and Chandler, M., "DNA Sequence at the End of IS1 Required for Transposition," <u>Nature</u> 317(6036):458-460 (1985).
- 35. Prentki, P., Teter, B., Chandler, M. and Galas, D., "Functional Promoters Created by the Insertion of Transposable element IS1," J. Mol. Biol. 191(3):383-393 (1986).
- 36. Gamas, P., Burger, A.C., Churchward, G., Caro, L., Galas, D. and Chandler, M., "Replication of pSC101: Effects of Mutations in the *E. coli* DNA binding Protein IHF," <u>Mol Gen Genet</u>, 204(1):85-89 (1986).
- 37. Prentki, P., Gamas, P., Chandler, M. and Galas, D., "Functions of the Ends of IS1," <u>Replication and</u> <u>Recombination of DNA</u>, Kelly *et al.*, (eds.), Alan R. Liss, Inc. pp. 719-734 (1987).
- Gamas, P., Chandler, M., Prentki, P. and Galas, D., "E. coli Integration Host Factor Binds Specifically to the Ends of the Insertion Sequence IS1 and to its Major Insertion Hot-Spot in pBR322," <u>J Mol Biol</u>, 195:261-272 (1987).
- 39. Gamas, P., Caro, L., Galas, D. and Chandler, M., "Expression of F Transfer Functions Depends on the *E. coli* Integration Host Factor," <u>Mol Gen Genet</u>, 207:302-305 (1987).
- 40. Prentki, P., Chandler, M. and Galas, D., *"E. coli* Integration Host Factor Bends the DNA at the Ends of IS1 and in an Insertion Hotspot with Multiple IHF Binding Sites," <u>EMBO J</u>, 6:2479-2487 (1987).
- 41. Prentki, P., Pham, M.H., Gamas, P., Chandler, M. and Galas, D., "Artificial Transposable Elements in the Study of Insertion Sequence IS1," <u>Gene</u>, 61:91-101 (1987).
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PATENTS

<u>Issued</u>

- 1. Nucleic acids encoding a novel family of TGF-beta binding proteins from humans U.S. Patent No. 6,395,511; May 28, 2002
- 2. Chromosome 1 gene and gene products related to Alzheimer's disease U.S. Patent No. 6,468,791 B1; October 22, 2002
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- 6. Methylation Analysis Using Nicking Agents U.S. Patent No. 6,884,586; April 26, 2005
- 7. Nucleic acid amplification using nicking agents U.S. Patent No. 7,112,423; September 26, 2006
- 8. Methods for modulating bone mineralization U.S. Patent No. 7,192,583; March 20, 2007
- 9. Compositions and methods for increasing bone mineralization U.S. Patent No. 7,572,899; August 11, 2009
- 10. Antibodies associated with alterations in bone density U.S. Patent No. 7,758,858; July 20, 2010
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- 12. Compositions and methods for increasing bone mineralization U.S. Patent No. 7,994,299; August 9, 2011
- 13. Improved methods to detect and quantify RNA WO Patent 2,012,112,714; August 24, 2012
- 14. Diagnosis and treatment of chronic lymphocytic leukemia (CLL) WO Patent 2,012,129,126; September 28, 2012
- 15. Diagnosis and treatment of chronic lymphocytic leukemia (CLL) U.S. Patent 20,120,252,871; October 4, 2012
- 16. Methods to detect and quantify RNA U.S. Patent 20,120,283,106; November 8, 2012
- 17. Methods and compositions for profiling RNA molecules EP Patent 2,531,612; December 12, 2012
- Methods and compositions for profiling RNA molecules U.S. Patent 20,130,059,736; March 7, 2013
- 19. Compositions and Methods for Increasing Bone Mineralization U.S. Patent 20,130,121,995; May 16, 2013

FUNDING

Current

Role: Sub-award Investigator (Julie Saugstad, PI / OHSU), NIH/NIA RO1 Award No. AG079356-01A1 *Human Cerebrospinal Fluid Extracellular Vesicles: Utility as Disease Specific Biomarkers and Impact on Alzheimer's Disease Pathology* - The goal of this study is to combine the physical features, surface markers, and cargo in human cerebrospinal fluid extracellular vesicles to establish specific biomarkers for AD, and to elucidate the molecular mechanisms underlying extracellular vesicle-mediated AD pathogenesis.

Status: Funded 04/15/23 - 02/28/28

Role: Co-Principal Investigator, NIH Award No. 1U54DA049098-01

exRNA Data Management Research Repository (DMRR), PHASE II

This is the data management, analysis, repository, and scientific outreach project for the ECRP Consortium program, funded under the NIH Common Fund. The author is one of three PI's for the DMRR, leading the Scientific Outreach component, and participating in the computational data analysis component.

Status: Funded 08/15/19 - 07/31/23

Recent Past

Role: Co-Principal Investigator, Indivumed Collaboration

Development of a Big Data Analytics Approach on the IndivuType[™] Portal for cancer research: The goal of the collaboration is to develop an automated approach based on methods and algorithms developed by PNRI (Sakhanenko, Galas and colleagues,2014-2017) to identify dependencies between clinical outcome variables and molecular predictors in Indivumed's multi-omics Data. Based on the results, the approach will be used in an effort to identify commercially viable targets and/or for outcome prediction based on the dependencies identified, which may be implemented as a component of the IndivuType[™] data analysis portal.

Status: Funded 07/01/19 to 08/01/22

Role: Principal Investigator, NIH Award No. 1U01HL126496

Reference Profiles of Extracellular RNA in 4 Body Fluids of Healthy Humans

This project is focused on developing and applying methods for RNA-seq, protocols and calibration, and sequence analysis. In addition to the methods the output will be exogenous RNA profiles from four different body fluids, serum, plasma, CSF and saliva, drawn from the same healthy subjects at the same time using NextGen RNA-seq.

Status: Funded 08/01/14 to 07/31/19

Role: Co-Principal Investigator, NIH Award No. 1U54DA036134-01

exRNA Data Management Research Repository (DMRR)

This is the data management, analysis and repository, and scientific outreach project for the ECRP Consortium program. The author is one of three PI's for the DMRR, leading the Scientific Outreach component, and participating in the computational analysis component.

Status: Funded 08/01/13 to 07/31/18

Role: Principal Investigator, NIH Award No. 3U01HL126496-04S1 Reference Profiles of Extracellular RNA in 4 Body Fluids of Healthy Humans - SUPPLEMENT The goal of this supplemental proposal is to characterize the small RNA spectrum of non-vesicle-encapsulated circulating RNAs. This proposal complements our original U01 proposal to profile the small RNA spectrum of whole body fluids and of small RNAs contained specifically in lipid vesicles in those fluids. With this supplemental proposal, we will be able to characterize not only the small RNA profile of the whole body fluid, but also the distribution of small RNAs between vesicle and nonvesicle compartments.

Status: Funded 09/15/17 to 04/30/18

<u>Past</u>

Role: Principal Investigator, Award No. OPP1126103 - Supplement

Bill & Melinda Gates Foundation: Information-Theory Approach to Childhood Development Data These are supplemental funds for our initial two-year project to apply new Information Theory-based analysis methods to complex, multi-variable child development data in order to better understand key dependencies without the limits of model-dependent assumptions.

Status: Funded 04/01/17 - 12/31/17

Role: Principal Investigator, Award No. OPP1126103

Bill & Melinda Gates Foundation: Information-Theory Approach to Childhood Development Data The aim of this two-year project is to apply new Information Theory-based analysis methods to complex, multivariable child development data in order to better understand key dependencies without the limits of modeldependent assumptions.

Status: Funded 03/17/15 - 03/31/17

Role: Principal Investigator, USF/Helmsley Foundation Subagreement Award No. 6119-1370-00-B

"Integrated Information Theory and Rule-based Methods for High-Throughput Pattern Discovery in TEDDY Study Data Analysis" This project will combine our information theory and Rule-based approaches to create a method capable of taking very large data sets and extracting key sets of complex "rules" to detect complex multivariable dependencies implied by the longitudinal TEDDY data set.

Status: Funded 09/01/15 to 06/31/17

Role: Principal Investigator, NSF/EAGER Award No. IIS-1340619

"Information and complexity in the analysis of biological data sets and networks"

This small two-year project is based on previous work and proposals for biological complexity measures and their relationships to quantitative biological information. This work is entirely theoretical, and computational in nature.

Status: Funded 07/01/13 to 06/30/15

Role: Principal Investigator, University of Luxembourg – Institute for Systems Biology Research Program, a program whose goal is to develop a Center for Systems Biomedicine at the University of Luxembourg and carry out collaborative research in "Systems Genetics and Molecular Phenotyping"

Status: Funded for 1/1/09 to 12/31/13, Research and "knowledge transfer" funding of ~\$98MM.

Role: Principal Investigator (4 co-PI's, 2 external participants) "Structure and Origins of Functional Modules in Yeast", National Science Foundation Status: Funded for \$4.88MM, 9/1/05 -8/31/10

Role: Principal Investigator of Battelle Memorial Institute Bioinitiative focused on Systems biology of Pulmonary Disease

Status: Year 1 (2007), \$3.5MM; Year 2 (2008), \$4.5MM, Year 3, \$3.7MM

Role: Principal Investigator "Isothermal Chain Reaction Research", Defense Advanced Research Projects Agency DARPA Status: Funded for \$489,500; 07/01/02 - 09/30/03

Role: Senior Participant "Partnerships for Innovative Bioscience Entrepreneurs," PI – David Finegold, KGI National Science Foundation Status: Funded for \$600,000; 08/01/03 – 07/31/06

Role: Principal Investigator "Handheld Isothermal Silver Standard Sensor" Ionian / DARPA Status: Funded for \$489,400; 01/09/04 – 01/08/05

Role: Subcontractor Northrop Grumman / Ionian / HSARPA TTA-1 "Area Detector and Related Technology"

Role: Subcontractor Ionian / HSARPA TTA-2 "HVAC Detector and Related Technology"

Role: Co-PI

"ITR: A Twin-Framework to Analyze, Model and Design Robust, Complex Networks Using Biological and Computational Principles," PI - Animesh Ray. National Science Foundation - Information Technology Research (ITR) Status: Funded for \$2,040,361; 09/01/02 - 08/31/05 Role: Co-PI "Causes of robustness and vulnerability in real-world networks: Lessons from molecular biology," PI - Animesh Ray. National Science Foundation - Quantum and Biologically Inspired Computing (QuBIC) Status: Funded for \$501,105; 09/01/01 - 08/31/05

Previous funding has included 13 years continuous funding of an NIH RO1 grant (NIAID) on DNA Transposition, NSF grants and other funding from NIH, DARPA, the Norris Foundation and the Keck Foundation