BIOGRAPHICAL SKETCH

NAME: Goldman, Robert David

eRA COMMONS USER NAME (credential, e.g., agency login): r-goldman

POSITION TITLE: Professor, Cell and Developmental Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Vermont	B.A., M.S.	1961, 1963	Zoology
Princeton University	M.S., Ph.D.	1967	Biology
Royal Postgraduate Medical School, London	Postdoctoral	1968	Enzyme Cytochemistry and Cell Biology
MRC Institute of Virology, Glasgow	Postdoctoral	1968	Cell Biology

A. Personal Statement

I have been committed to studying the structure and function of Intermediate Filaments (IF) since 1970. Our laboratory studies both the cytoskeletal and nucleoskeletal networks of IF. With respect to the cytoskeletal systems, our studies have involved the regulation of their assembly states and their roles in establishing and maintaining cell shape and mechanical integrity. We have also determined their dynamic properties emphasizing their roles in cell motility, adhesion, intracellular organelle movements and the positioning of organelles in different regions of the cytoplasm. In the early 1980s, the discovery by several labs, including my own, that lamins were the nuclear form of IFs, simply fascinated me. As a result, the nuclear lamins became a major focus of our research for over 30 years. During this period we have shown that these nuclear targeted IF proteins are involved in determining the size, shape and mechanical properties of the nucleus; and they are critically important factors in the disassembly and reassembly of the nucleus during cell division. We have also shown that the lamins provide a molecular scaffolding within the nucleus that plays a vital role in essential functions such as DNA replication, transcription and chromatin organization. In recent years our interest in the lamins has increased as more and more LA mutations have been reported; now numbering close to 500 and causing many different diseases. With respect to these mutations we have focused on those causing the premature aging disease Hutchison Gilford Progeria Syndrome and other atypical forms of progeria. This has led us into studies of the different structures formed by the A- and B-type lamins, their different roles in chromosome organization and positioning during interphase, and in their functions in epigenetic modifications of chromatin and replicative senescence. Over the many years that we have been studying both the nuclear lamins and the cytoskeletal forms of IF, we have developed an extensive array of techniques for assaying their functions, including a large collection of antibodies and molecular reagents that we have developed for both in vivo and in vitro analyses. My laboratory has encouraged many others to consider working on both the nucleoskeletal and cytoskeletal IF networks and is constantly supplying reagents to those interested in determining their functions. Likewise, over the years we have built up a strong network of collaborators in the US and Europe who provide expertise and reagents that advance our research.

B. Positions and Honors

Positions and Employment

1969-1973 Assistant Professor of Biology, Case Western Reserve University.
1973 Visiting Scientist, Imperial Cancer Research Fund Laboratories, London.
1973-1974 Visiting Scientist, Cold Spring Harbor Laboratory
1976- Investigator, Whitman Center, Marine Biological Laboratory
1973-1981 Associate Professor and Professor of Biological Sciences, Carnegie-Mellon University.
1981-10/2019 The Stephen Walter Ranson Professor and Chair, Department of Cell and Molecular Biology, Feinberg School of Medicine, Northwestern University.

2019-present Professor of Cell and Developmental Biology, Stephen Walter Ranson Professor Emeritus, Feinberg School of Medicine, Northwestern University

Other Experience and Professional Memberships (Selected)

1978 Member, National Institutes of Health Molecular Cytology Study Section.
1979-1983 Member, National Institutes of Health Cell Biology Study Section.
1980 Chairman, Committee on Scientific Programs, American Society for Cell Biology.
1981-1988 Instructor and Director, Physiology Course at the Marine Biological Laboratory.
1986-1990 Member, Council of the American Society for Cell Biology.
1986-1996 Member, Board of Trustees, Marine Biological Laboratory, Woods Hole MA.
1988-1992 Member, American Cancer Society Personnel Committee B.
1988-1997 Founder and First Chair, Public Information Committee, American Society for Cell Biology.
1990-1995 Director and Founder, Science Writers Hands-On Lab Course, Marine Biological Laboratory.
1997-2001 Board of Directors, American Association for the Advancement of Science.
2010-present Emeritus Member Board of Trustees, MBL, Woods Hole
2001-2012 Member, Juvenile Diabetes Foundation Stem Cell Advisory Committee.
2002-2006 Trustee, The Keith R. Porter Endowment for Cell Biology.
2003 Member, NIH Reorganization of Study Sections in Cell Biology Meeting.
2003-2012 Director, Whitman Research Center, Marine Biological Laboratory.
2005- Associate Editor, FASEB Journal.
2006- Editorial Advisory Board, Cold Spring Harbor Laboratory Manuals.
2007-2009 Member, Executive Committee, American Society for Cell Biology.
2007-2010 Advisory Committee, Progeria Research Foundation.
2009-2012 Member, Scientific Advisory Board of the Institute of Medical Biology, Singapore.
2009- Editorial Board, Nucleus.
Associate Editor, Molecular Biology of the Cell.
Associate Editor, BioArchitecture.
2013- Member, Euro-BioImaging Independent Evaluation Board.
Editorial Board, Aging Cell.
2014- Member Research Advisory Committee, National Center for Microscopy and Imaging Research, UCSD.
2017 Co-editor (T. Pollard). The Cytoskeleton. Cold Spring Harbor Press (2017).

Honors

1963-1967 The John Sterry Fellow and NIH Predoctoral Fellow, Princeton University.
1967-1969 American Cancer Society Eleanor Roosevelt Fellow at the Royal Postgraduate Medical School, London, and the MRC Institute of Virology, Glasgow.
1988 Fellow, American Association for the Advancement Science.
1992 President, American Association of Anatomy, Cell Biology and Neuroscience Chairpersons.
1999-2009 Merit Award, National Institute for General Medical Science.
2005-2008 Ellison Foundation Senior Scholar.
2008 President, American Society for Cell Biology.
Accomplished Undergraduate Alumnus, Department of Biology, University of Vermont.
Gordon Conference on Intermediate Filaments Vice Chair (2010), Chair (2012).
2013 Recipient of the Charles University Medal for Outstanding Scientific Achievement, Prague.
2015 Elected member of the Finnish Society for Sciences and Letters.
2016 Elected an Inaugural Fellow of the American Society for Cell Biology.
2018 Awarded the title of Doctor of Medical Sciences, honoris causa from Charles University, Prague

Recent Lectures (selected)

2015 Symposium Speaker, European Intermediate Filament Workshop, Stockholm.
Lecture, University of Helsinki Biocenter, Helsinki
Honorary Lecture, Finnish Society for Sciences and Letters, Helsinki.
The Frontiers of Science Lecture, University of Turku Biocenter, Turku, Finland.
Symposium Speaker, H.C. Jacobaeus Symposium, Turku Graduate School of Biomedical Sciences, Finland.
Speaker, Nuclear Envelope Dynamics Subgroup, ASCB Annual Meeting, San Diego.
2016 Speaker and Co-chairman, Lamin Session, Cold Spring Harbor Meeting on Nuclear Organization and Function, Cold Spring Harbor NY.
Nobel Minisymposium on Progeria, Stockholm.

Speaker, Progeria Research Foundation Scientific Workshop, Boston.
Keynote Lecture, Gordon Research Seminar on Intermediate Filaments, Stowe VT.
Speaker, Gordon Research Conference on Intermediate Filaments, Stowe VT.
Keynote Lecture, 12th Intl. Congress of Cell Biology, Prague, Czech Republic.
Symposium Speaker, ICCB Cell Biology Education Symposium, Prague, Czech Republic.

2017 Speaker, Session on Nuclear Structure and Function, American Society for Biochemistry and Molecular Biology Annual Meeting, Chicago.
Keynote Lecture, and Session 3 Chair, COST School and The Batsheva de Rothschild Seminar on the Nuclear Lamina and Nuclear Organization, Yearim-Judean Hills, Israel.
Speaker, Uno Lindberg Memorial Symposium, Stockholm.

2018 Plenary Speaker, ICCB 2018 Intl. Congress of Cell Biology, Hyderabad, India.
Panel Member, Cell Biology Education, ICCB 2018 Intl. Congress of Cell Biology, Hyderabad.
Symposium Speaker, 43rd FEBS Congress (Federation of European Biological Societies), Prague, Czech Republic.
Speaker, Gordon Research Conference on Intermediate Filaments, Lucca (Barga), Italy.
Lecture, Annual Retreat & Symposium, Pennsylvania Muscle Institute, Philadelphia.

2019 Keynote Lecture, Gordon Research Conference on Motile and Contractile Systems, New London NH.
Keynote Speaker, 11th European Meeting on Intermediate Filaments, Turku, Finland.
Speaker, Waterman Symposium: Cell Machines at Work, National Institutes of Health, Bethesda MD.
Speaker, Gruenbaum Special Symposium, Hebrew University of Jerusalem, Israel.

2020 Keynote Speaker, EMBO Workshop on Chromatin Structure, Organization and Dynamics, Prague, Czech Republic

C. Contribution to Science

1. In the 1970's there was controversy over whether Intermediate filaments (IF) were a separate class of cytoskeletal polymer, with some cell biologists suggesting they were 'mini-tubules' (i.e. small microtubules). To demonstrate that 10 nm IF were a third cytoskeletal system we carried out studies describing their unique properties in cells; their isolation and biochemical characterization; and the conditions for polymerizing their subunits into 10 nm IF in vitro. These early studies were essential for demonstrating that IF were a distinct class of cytoskeletal polymers.
   a. Goldman, R.D.& Follett, E.A.C. (1970). Birefringent filamentous organelle in BHK-21 cells and its possible role in cell spreading and motility. Science Jul 17;169:286-288. PMID: 4915821
   b. Starger, J.M.& Goldman, R.D. (1977). Isolation and preliminary characterization of 10nm filaments from baby hamster kidney (BHK-21) cells. Proceedings of the National Academies of Science USA 74(6):2422-2426. PMCID: PMC432184
   c. Zackroff, R.V. & Goldman, R.D. (1979). *In vitro* assembly of intermediate filaments from baby hamster kidney (BHK-21) cells. Proceedings of the National Academies of Science USA 76(12):6226-6230. PMID: 293716 PMCID: PMC411836
   d. Zackroff, R.V., Idler, W.W., Steinert, P.M. & Goldman, R.D. (1982). *In vitro* reconstitution of intermediate filaments from mammalian neurofilament triplet polypeptides. Proceedings of the National Academies of Science USA Feb;79(3):754-757. PMID: 6950425 PMCID: PMC345830

2. For many years IF were considered to be static constituents of the cytoskeleton. However, our early microscopic studies demonstrated that this was not the case. Using polarized light, electron microscopy and immunofluorescence we revealed that IF networks were very dynamic. We demonstrated significant organizational changes in their assembly states during cell division, cell spreading and cell shape transitions. Other studies utilizing the microinjection of purified and biotinylated or fluorescently tagged forms of IF, and more recently the expression of GFP-tagged IF proteins revealed that IF subunits continuously exchange in living cells. Other discoveries revealed that small assemblies of IF were actively moved bi-directionally, driven by microtubule motors. Because there are no drugs or reagents similar to colchicine or cytochalasin that can be used to disrupt/depolymerize IF, we also developed the use of mimetic peptides as an alternate way to drive disassembly of IF in vivo. Recently our studies on the rare human disorder Giant Axonal Neuropathy have provided new insights into the mechanisms responsible for the degradation and turnover of IF proteins.
   a. Vikstrom, K.L., Borisy, G.G. & Goldman, R.D. (1989). Dynamic aspects of intermediate filament networks in BHK-21 cells. Proceedings of the National Academies of Science USA Jan;86(2):549-553. PMID: 2643116 PMCID: PMC286509

b. Goldman, R.D., Khuon, S., Chou, Y.H., Opal, P. & Steinert, P.M. (1996). The function of intermediate filaments in cell shape and cytoskeletal integrity. Journal of Cell Biology Aug;134(4):971-983. PMID: 8769421 PMCID: PMC2120965
c. Prahlad, V., Yoon, M., Moir, R.D., Vale, R.D. & Goldman, R.D. (1998). Rapid movements of vimentin on microtubule tracks: kinesin-dependent assembly of intermediate filament networks. Journal of Cell Biology 143:159-170. PMID: 9763428 PMCID: PMC213817
d. Mahammad, S., Murthy, P.S.N., Didonna, A., Grin, B., Israeli, E., Perrot, R., Bomont, P., Julien, J-P, Kuczmarski, E., Opal, P. & Goldman, R.D. (2013) Giant axonal neuropathy-associated gigaxonin mutations impair intermediate filament protein degradation. Journal of Clinical Investigation May 1;123(5):1964-1975. doi: 10.1172/JCI66387. Apr 15: Epub. PMID 23585478 PMCID: PMC3635735.

3. My lab has also worked to understand how IF assembly is regulated and how IF contribute to the mechanical properties of the cell. We discovered that a major means of regulation involves reversible phosphorylation of specific serine residues of vimentin and importantly that the disassembly that takes place during mitosis is regulated by cdk1 kinase. In addition, we discovered that the early steps in the assembly of IF are coupled to the translation of their mRNAs in a process called dynamic co-translation. With regard to the regulation of the cell's mechanical properties, we have collaborated in studies to determine how shear forces cause changes in IF organization and how these changes regulate cytoplasmic stiffness.
   a. Chou, Y.H., Bischoff, J.R., Beach, D. & Goldman, R.D. (1990). Intermediate filament reorganization during mitosis is mediated by $p34^{cdc2}$ phosphorylation of vimentin. Cell Sep 21;62(6):1063-1071. PMID: 2169348
   b. Chang, L., Shav-Tal, Y., Trcek, R., Singer, R.H. & Goldman, R.D. (2006). Assembling an intermediate filament network by dynamic cotranslation. Journal of Cell Biology Feb 27;172(5):747-758. PMID 16505169 PMCID: PMC2063706
   c. Hu J, Li Y, Hao Y, Zheng T, Parada G, Wu H, Lin S, Wang S, Zhao X, Goldman R, Cai S and Guo M. (2019). High stretchability, strength and toughness of living cells enabled by hyperelastic vimentin network. PNAS 116(35): 17175-17180 PMID:31409716 PMCID:PMC6717279
   d. Patteson, A.E., Vahabikashi, A., Pogoda K., Adam, S.A., Mandal, K., Kittisopikul, M., Sivagurunathan, S., Goldman, A., Goldman,R. and Janmey, P.A. (2019) Vimentin protects cells against nuclear rupture and DNA damage during migration. J Cell Biol. Nov 4, 2019 Vol 218, No. 11 PMID: 31676718 DOI: 10.1083/jcb.201902046

4. We demonstrated that vimentin IF regulate different aspects of cell motility. Within cells we showed that IF regulate the movements and positioning of melanosomes and mitochondria. Studies on the epithelial to mesenchymal transition (EMT) have revealed that vimentin IF play essential roles in the head to tail polarity and shape of moving fibroblasts; and they have a crucial role in establishing the leading edge of the migrating cell.
   a. Chang, C., Barlan, K., Chou, Y.H., Grin, B., Lakonishok, M., Serpinskaya, A.S., Shumaker, D.K., Herrmann, H., Gelfand, V.I. & Goldman, R.D. (2009) The dynamic properties of intermediate filaments during organelle transport. Journal of Cell Science Aug 15;122(Pt 16):2914-2923. PMID: 19638410 PMCID: PMC2724608
   b. Mendez, M.G., Kojima, S.I. & Goldman, R.D. (2010) Vimentin induces changes in cell shape, motility and adhesion during the epithelial to mesenchymal transition. FASEB Journal Jun;24(6): 1838-1851. Jan 22: Epub. PMID: 20097873 PMCID: PMC2874471
   c. Nekrasova, O.E., Mendez, M.G., Chernoivanenko, I.S., Tyurin-Kuzmin, P.A., Kuczmarski,E.R., Gelfand, V.I., Goldman, R.D. & Minin, A.A. (2011) Vimentin intermediate filaments modulate the motility of mitochondria. Molecular Biology of the Cell Jul;22(13):2282-2289. May 11: Epub. PMID 21562225 PMCID: PMC3128530
   d. Helfand, B.T., Mendez, M.G., Murthy, P.S.N., Shumaker, D.K., Grin, B., Mahammad, S., Aebi, U., Wedig, T., Wu. Y.I., Hahn, K.M., Inagaki, M., Herrmann, H. & Goldman, R.D. (2011) Vimentin organization modulates the formation of lamellipodia. Molecular Biology of the Cell Apr;22(8):1274-1289. Feb 23: Epub. PMID 21346197 PMCID: PMC3078081

5. We carried out the early studies on the nuclear lamins, and were the first to suggest that they were IF proteins which assembled into paracrystals in vitro. We developed techniques for demonstrating that they were dynamic components of the nucleus in interphase and were present both in the lamina and nucleoplasm. Functional assays revealed that lamins play important roles in DNA synthesis and in regulating RNA pol II. We were the first to demonstrate that the A-type lamins played an important role in the location and regulation of peripheral heterochromatin using progeria patient cells and that lamin B1 was

an important biomarker for cellular senescence. Our studies have shown that the A and B type lamins have distinctly different structures and functions.

a. Stephens AD, Liu PZ, Kandula V, Chen H, Almassalha LM, Herman C, Backman V, O'Halloran T, Adam SA, Goldman RD, Banigan EJ and Marko JF. (2019) Physicochemical mechanotransduction alters nuclear shape and mechanics via heterochromatin formation. MBoC Jun 19:mbcE19050286T. DOI: 10.1091/mbc.E19-05-0286-T PMID: 31216230
b. Shimi, T., Butin-Israeli V., Adam, S.A., Hamanaka, R.B., Goldman, A.E., Lucas, C.A., Shumaker, D.K., Kosak, S.T., Chandel, N.S. & Goldman, R.D. (2011) The role of nuclear lamin B1 in cell proliferation and senescence. Genes and Development Dec 15;25(24):2579-2593. Dec 8: Epub. PMID: 22155925 PMCID: PMC3248680
c. Shimi, T., Kittisopikul, M., Tran, J., Goldman, A.E., Adam, S.A., Zheng, Y.Z., Jaqaman, K. & Goldman, R.D. (2015) Structural organization of nuclear lamins A, C, B1 and B2 revealed by super-resolution microscopy. Molecular Biology of the Cell (Special Issue on Quantitative Biology) Nov 5;26(22):4075-4086. Aug 26: Epub. PMID: 26310440 PMCID: PMC4710238
d. Turgay, Y, Eibauer, M., Goldman, A.E., Shimi, T., Khayat, M., Ben-Harush, K., Dubrovsky-Gaupp, A., Sapra, K.T., Goldman, R.D. and Medalia, O. (2017) The molecular architecture of lamins in somatic cells. Nature Mar;543(7644):261-264. PMID:28241138 PMCID: PMC5616216

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/robert.goldman.1/bibliography/40685504/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

R01 GM106023-08 Goldman (PI) 04/01/2017--12/31/2020
NIH-NIGMS
Analysis of Lamin-chromatin Interactions and their Regulation of Chromosome Organization and Gene Expression.
Determination of the roles of the nuclear lamin proteins in organizing and regulating the genome. The studies proposed in this grant use high-resolution techniques to determine how the nuclear structures formed by the lamins regulate the organization of the genome in both healthy and diseased cells.

P01 HL071643-11A1 (PI: Sznajder) 09/01/2015-06/30/2020
NIH/NHLBI (Project 2 Lead: Ridge)
PPG: Pathophysiology of Alveolar Epithelial Lung Injury.
Project 2: Role of Intermediate Filaments in Acute Lung Injury.
The major goal of this project is to test the hypothesis that vimentin acts as a scaffold for the assembly and activation of the NLRP3 inflammasome and that NOD2 protein interaction with vimentin is required for the activation of IRF3 signaling.
Role: Co-Investigator

U54 CA193419 (PI: O'Halloran) 05/01/2015--04/30/2020
Spatio-Temporal Organization of Chromatin and Information Transfer in Cancer.
NIH/NCI
Project 3: Goal of this award is to facilitate collaboration on the mechanical properties of the nucleus with Prof. John Marko of the Physics Department.
Role: Co-Investigator

2 P01 GM096971-06 Goldman (PI) 06/05/2011—07/31/2022
Regulation and Function of Intermediate Filaments in Cell Mechanics.
Determination of how alterations in the assembly states and mechanical properties of cytoskeletal IF, specifically vimentin (VIF), regulate the micromechanical properties of cells in response to mechano- and chemo-signaling.