BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Sobel, Mark E.

eRA COMMONS USER NAME (agency login): MESOBEL

POSITION TITLE: Executive Officer

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Brandeis University, Waltham, MA	BA	1970	Psychology
Mount Sinai School of Medicine, New York, NY	MD	1975	Medicine
Graduate School of the City University of New York, New York, NY	PHD	1975	Biomedical Sciences
Boston Children's Hospital Medical Center, Boston, MA	Resident	1976	Pediatrics
National Cancer Institute, NIH, Bethesda, MD	Postdoctoral Fellow	1980	Molecular Biology

A. Personal Statement

I have a career-long interest in deciphering the pathogenesis of cancer and developing improved diagnostic, prognostic, and therapeutic approaches to neoplastic and other diseases and disorders. I was an intramural scientist at the National Institutes of Health (primarily the National Cancer Institute) from 1976 to 2001. In 2001, I was appointed as the Executive Officer of the American Society for Investigative Pathology (ASIP) and retired from the US Public Health Service. My research projects at the NIH focused on differential gene expression in cancer, leading me to explore the interactions of the cancer cell with the extracellular matrix, especially the basement membrane. I was one of the original cloners of the interstitial and basement membrane collagens in the 1970s and early 1980s. My research on the interactions of metastatic cancer cells with laminin led to studies on tumor invasion and the cloning of a non-integrin laminin receptor, a multifunctional protein that is also a ribosomal binding protein. A second major initiative was elucidation of mechanisms of suppression of tumor metastasis and discovery of a metastasis suppressor gene (NM23). Both the laminin receptor and NM23 projects resulted in patents. [Sobel et al: Recombinant DNA Clone encoding Laminin Receptor, Patent #4,861,710 (1989); Steeg et al: Diagnosis of Metastatic Potential of Tumors by the NM23 gene, Patent #5,049,662 (1991)]. These projects are outlined in more detail in Part C, Contribution to Science.

I was an “early adopter” of molecular diagnostics. I co-developed the Concepts in Molecular Biology Course for ASIP in 1987 and was the Director of the course from 1988-1999. Over 2,500 scientists completed the four-day course over a twelve-year period. I have continued to teach on advances in molecular diagnostics and the utilization of human biological samples in research, with an emphasis on ethical considerations and served as the Director of Continuing Medical Education (CME) Programs at ASIP.

For the past 20 years, I have focused my attention on biomedical ethics, human subjects protections, and the application of molecular diagnostics to improving healthcare. I have been a major spokesperson within the pathology community to educate and discuss appropriate means for clinicians and researchers to access human biological materials to improve knowledge about human disease and simultaneously respect human subjects. I was a member of the Board of Directors of AAHRPP from its inception in 2001 until 2008.

B. Positions and Honors

Positions and Employment

1980 - 1983 Research Associate, National Institute of Dental Research, Laboratory of Developmental Biology and Anomalies, Bethesda, MD

1983 - 1992 Senior Investigator, National Cancer Institute, NIH, Laboratory of Pathology, Bethesda, MD

1992 - 2001 Chief, NCI, NIH, Laboratory of Pathology, Bethesda, MD
2001 - 2018 Executive Officer, American Society for Investigative Pathology (ASIP), Bethesda, MD
2001 - 2018 Executive Officer, Intersociety Council for Pathology Information (ICPI), Bethesda, MD
2001 - 2011 Executive Officer, Association for Molecular Pathology (AMP), Bethesda, MD
2001 - 2011 Executive Officer, Association of Pathology Chairs, Bethesda, MD
2001 – 2012 Guest Researcher/Special Volunteer, NCI, NIH, Laboratory of Pathology, Bethesda, MD
2011 - present Executive Officer Emeritus, AMP
2018 – present Executive Officer Emeritus, ASIP, ICPI

Other Experience and Professional Memberships

1976 - present Member, American Association for the Advancement of Science
1977 - present Member, American Association for Cancer Research
1987 - Co-director, Concepts in Molecular Biology Course, American Association of Pathologists
1987 - Member, Minority Recruitment Networking Task Force, National Cancer Institute
1987 - present Member, American Society for Investigative Pathology
1988 - present Member, American Society for Biochemistry and Molecular Biology
1988 - Member, Ad hoc, NIH Pathobiochemistry Study Section
1988 - 1999 Director, Concepts in Molecular Biology Course, American Society for Investigative Pathology
1989 - 2004 Consultant, Molecular Pathology Committee, College of American Pathologists
1990 - 1995 Chair, Education Planning Committee, American Society for Investigative Pathology
1991 - Organizer, Molecular Pathology Workshop, Annual Meeting of American College of Veterinary Pathologists
1992 - 1998 Member, Area Committee on Molecular Methods, NCCLS
1994 - Member, Organizing Committee, Molecular Diagnostics Workshop, UAREP
1994 - 1995 Organizer, Stowell Symposium, ASIP 1995 Annual Meeting at Experimental Biology 1995
1995 - present Member, Association for Molecular Pathology
1996 - Member, Ad hoc, NIDR, Oral Cancer Center Study Section
1996 - Member, Advisory Committee on Informed Consent, NHLBI
1996 - 1999 Member, Ad hoc Pathology Consensus on Stored Tissue Committee, College of American Pathologists
1996 - 2000 Associate Editor, Diagnostic Molecular Pathology
1997 - 1998 Chair, NIH Intramural Working Group on Studies Using Existing Human Samples or Data
1998 - present Member, Editorial Board, Laboratory Investigation
1998 - 2001 Member, Trans-NIH Group on Issues Related to Human Specimen Resources
1998 - 2001 Member, Trans-NIH Bioethics Committee
1999 - 2000 Visiting Professor, George Washington University Medical School, Pathology Department
1999 - 2001 Member, Ad hoc Committee on Genetics and Medical Information Privacy, College of American Pathologists
2000 Organizer, Chair, and Speaker, Presidential Symposium (“Molecular Markers of Cancer”), ASIP 2000 Annual Meeting at Experimental Biology,
2000 - 2001 NIH Representative, DHHS Working Group on Use of Human Biological Materials
2001 - present Member, United States and Canadian Academy of Pathology
2001 - 2008 Member, Board of Directors, Association for the Accreditation of Human Research Protection Programs, and Executive Committee (2003 – 2007)
2002 - Course Director and Lecturer, Introduction to Molecular Biology, Annual Meeting of the Society for Nuclear Medicine
2002 - Organizer and Moderator, Symposium on Molecular Surgical Pathology: Studies in Wax, Annual Meeting of the United States and Canadian Academy of Pathology
2002 - 2004 Member, Association of American Medical Colleges Council of Academic Societies Program Committee
2003 - 2004 Organizer and Chair, Symposium on Human Research Protections, Experimental Biology
2005 - present Director, ASIP Journal Continuing Medical Education Program

2005 - 2007	Member, National Library of Medicine Working Group, NIH Policy for Enhanced Public Access
2005 - 2008	Faculty, Current Applications of Molecular Pathology: Diagnosis and Implications for Therapy in Tissue Samples, Madrid, Spain
2005 - 2015	Senior Executive Advisory Board, Archives of Pathology and Laboratory Medicine
2007 - 2013	Member, PubMed Central National Advisory Committee of the National Library of Medicine
2008 - present	Member, FASEB Human Subjects Protections Advisory Committee
2009 -	Member, NINCDS Special Study Section for Biorepository Contracts
2009 -	Visiting Faculty, International Bioethics Course, Udine, Italy
2009 - 2010	Member, NICHD Special Study Section for Biorepository Contracts
2010 - present	Member, Advisory Board, NICHD Brain Trust
2010 - present	Member, Scientific Advisory Board, Canadian Prostate Cancer Biomarker Network
2010 -	Member, Department of Defense Study Section for Lung Cancer Repositories
2012 -	Member, Department of Defense Study Section for Lung Cancer Research Program
2012 -	Member, NIDDK Biosample Repository Contracts Review Panel
2013 -	Chair, NCATS Research Resource for Human Organs and Tissue Special Emphasis Panel
2013 -	Member, Bidirectional Research Round Table Meeting, NIDCR
2014	Organizer, Chair and Speaker, Stowell Symposium at ASIP 2014 Annual Meeting at EB
2014	Organizer and Chair, Plenary Session on Systems Biology, American College of Veterinary Pathologists Annual Meeting
2015 – 2019	Visiting Faculty, Curso Teórico-Práctico Intensivo de Biología y Patololgía Moleculares Para Médicos, Barcelona, Spain
2016	Chair, NIH Precisions Medicine Initiative Biorespository Study Section
2016 - 2017	Chair, NIDDK Biosample Repository Contracts Review Panel
2017	Chair, The Human Tissue and Organ Research Resource U42 Study Section, NIH Center for Scientific Review
2018	Member, NICHD National Children's Study Biological and Environmental Sample Repository Study Section
2018	Chair, NCI Special Emphasis Panel, Collaborative Human Tissue Netowork (CHTN)

Honors

1969	Phi Beta Kappa, Brandeis University
1969	John Leslie Award, Brandeis University
1970	Summa cum laude, Brandeis University
1975	Basic Sciences Achievement Award, Mount Sinai School of Medicine
1977	Sigma Xi, National Cancer Institute
1989	Commendation Medal, United States Public Health Service
1991	Saul J. Horowitz, Jr. Memorial Award, Mount Sinai School of Medicine
1995	Secretary-Treasurer, Association for Molecular Pathology
1995 - 1997	Councilor, American Society for Investigative Pathology (ASIP)
1995	Alpha Omega Alpha, Mount Sinai School of Medicine
1997 - 2000	Vice President-Elect, Vice President, and President, ASIP
1998 - 1999	President-Elect and President, Association for Molecular Pathology
2000	Highman Lecturer, University of California at Sacramento
2003 - 2007	Chair (elected), Intersociety Pathology Council
2006	Leadership Award, Association for Molecular Pathology
2007 - present	Chair (appointed), Intersociety Pathology Council
2013	Friend of Pathology, Association of Pathology Chairs
2017	Terry Ann Krulwich Physician Scientist Award, Icahn Mount Sinai School of Medicine

C. Contribution to Science

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1P3NrwxNkZbkA/bibliography/public/

1. Altered expression of connective tissue molecules in cancer and the cloning of interstitial and basement membrane-associated collagens and fibronectin.

As a post-doctoral fellow in the laboratory of Ira Pastan, National Cancer Institute from 1976-1979, I began an exploration of the differential expression of collagen and connective tissue (including basement membrane) molecules in in vitro and in vivo models of cancer. In the Pastan laboratory, I had the opportunity to utilize the first P3 containment lab at the National Cancer Institute and to develop methodologies for the isolation of long mRNA species. Our group cloned cDNAs of the α1 and α2 chains of type I collagen as well as fibronectin and discovered decreased levels of mRNAs for type I collagen and fibronectin in in vitro Rous sarcoma virus-chcik embryo fibroblasts. .

In 1980, I was given the opportunity to develop my own lab group in the Laboratory of Developmental Biology and Craniofacial Anomalies in the National Institute of Dental Research, and expanded my molecular explorations of collagens and connective tissue molecules. My laboratory cloned type II collagen and type IV collagen. We investigated the developmental and molecular biology of collagens in cartilage and bone formation and studied basement membrane molecular biology in a murine in vivo tumor system.

a. Sobel ME, Yamamoto T, Adams SL, DiLauro R, Avvedimento VE, de Crombrugghe B, Pastan I. Construction of a recombinant bacterial plasmid containing a chick pro- α2 collagen gene sequence. Proc Natl Acad Sci USA. 1978. 75:5846-5850.
b. Sobel ME, Yamamoto T, de Crombrugghe B, Pastan I. Regulation of procollagen messenger ribonucleic acid levels in Rous sarcoma virus-transformed chick embryo fibroblasts. Biochemistry. 1981. 20:2678-2684.
c. Vogeli G, Ohkubo H, Sobel ME, Yamada Y, Pastan I, de Crombrugghe B. Structure of the promoter for the chick alpha 2 collagen gene. Proc Natl Acad Sci USA. 1981. 78:5334-5338.
d. Fernandez MP, Young MF, Sobel ME. Methylation of type II and type I collagen genes in differentiated and dedifferentiated chondrocytes. J Biol Chem. 1985. 260:2374-2378.

2. The role of a non-integrin laminin receptor in cancer.

In 1983 I returned to the intramural program at the NCI as Senior Investigator in the Laboratory of Pathology. My group continued an exploration of connective tissue molecules in cancer with a focus on the role of the basement membrane in tumor invasion and metastasis. A 67-kDa laminin receptor had been isolated by Lance Liotta's group at the NCI and my laboratory used a monoclonal antibody to clone a cDNA probe (and eventually isolated the genomic clone) for a 37-kDa laminin receptor precursor. In 1989, we were awarded a patent from the US Patent and Trade Office: Sobel et al: Recombinant DNA Clone encoding Laminin Receptor, Patent #4,861,710. We discovered increased mRNA and protein expression in in vitro cancer cell lines and murine model systems as well as in human tissues. At the time, this work was controversial since integrins were discovered concurrently and the 67-kDa laminin receptor is a non-integrin. We eventually determined that the 37-kDa laminin receptor precursor was a multi-functional protein that also served as a ribosomal binding protein (p40), and was localized not only on the cell membrane but also in the nucleolus. The specific binding site for laminin was elucidated using cDNA-deduced synthetic peptides and was recently confirmed using the crystalline structure of the molecule by my former trainee, Nunzia Montuori (University of Naples, Italy), who continued to work on the project after I left the NCI.

a. Castronovo V, Colin C, Claysmith AP, Chen PHS, Lifrange E, Lambotte R, Krutzsch HC, Liotta LA, Sobel ME. Immunodetection of the metastasis-associated laminin receptor in human breast cancer cells obtained by fine needle aspiration biopsy. Am J Pathol. 1990. 137:1373-1381.
b. Castronovo V, Taraboletti G, Sobel ME. Laminin receptor complementary DNA-deduced synthetic peptide inhibits cancer cell attachment to endothelium. Cancer Res. 1991. 51:5672-5678.
c. Castronovo V, Taraboletti G, Sobel ME. Functional domains of the 67-kDa laminin receptor precursor. J Biol Chem. 1991. 266:20440-20446.
d. Campo E, Monteagudo D, Castronovo V, Claysmith AP, Fernandez PL, Sobel ME. Detection of laminin receptor mRNA in human cancer dell lines and colorectal tissues by in stiu hybridization. Am J Pathol. 1992. 141:1073-1083.

3. Suppression of tumor metastasis

Concurrent with the laminin receptor project, my group investigated the possibility that, just as there are tumor suppressor genes, there may be genes that suppress or inhibit tumor metastasis. Using differential

cDNA expression libraries we isolated a cDNA clone of the NM23 gene. In 1991, we were awarded a patent from the US Patent and Trade Office (Steeg et al: Diagnosis of Metastatic Potential of Tumors by the NM23 gene, Patent #5,049,662). My former post-doctoral fellow, Patricia Steeg, developed the NM23 project in her own lab when she became a Principal Investigator at NCI.

a. Sobel ME. Metastasis suppressor genes. J Natl Cancer Inst. 1990. 82:267-276.
b. Steeg PS, Bevilacqua G, Kopper L, Thorgeirsson UP, Talmadge JE, Liotta LA, Sobel ME. Evidence for a novel gene associated with low tumor metastatic potential. J Natl Cancer Inst. 1988. 233:200-203.
c. Steeg PS, Bevilacqua G, Pozzatti R, Liotta LA, Sobel ME. Expression of NM23, a gene associated with low tumor metastatic potential, is increased during adenovirus 2 E1a inhibition of experimental metastasis. Cancer Res. 1988. 48:6550-6554.
d. Bevilacqua G, Sobel ME, Liotta LA, Steeg PS. Association of low nm23 RNA levels in human primary infiltrating ductal breast carcinomas with lymph node involvement and other histopathological indicators of high metastatic potential. Cancer Res. 1989. 49:5185-5190.

4. Collaborations to investigate the molecular biology and differential gene expression in cancer and other disorders.

As one of the early adopters of molecular approaches I had the opportunity to collaborate with several scientists to provide molecular techniques and approaches to their own systems. At NCI, I collaborated with Michael Gottesman on the expression and cloning of the MDR1 gene, William Stetler-Stevenson on metalloproteinases, and Lance Liotta on autotaxin, among others. In addition, I collaborated with Fu-Tong Liu (Scripps Research Institute) on galectins, and Marian Young (National Institute of Dental and Craniofacial Research), my former post-doctoral fellow, on cloning and expression of amelogenin, among others.

a. Gottesman MM, Sobel ME. Tumor promoters and Kirsten sarcoma virus increase synthesis of a secreted glycoprotein by regulating levels of translatable mRNA. Cell. 1980. 19:449-455.
b. Shimokawa H, Sobel ME, Sasaki M, Termine JD, Young MF. Heterogeneity of amelogenin mRNA in the bovine tooth germ. J Biol Chem. 1987. 262:4042-4047,
c. Murata J, Lee HY, Clair T, Arestad AA, Sobel ME, Liotta LA, Stracke ML. cDNA cloning of the human tumor motility-stimulating protein, autotaxin, reveals a homology with phosphodiesterases. J Biol Chem. 1994. 269:30479-30484.
d. Castronovo V, van den Brule FA, Jackers P, Clausse N, Liu FT, Gillet C, Sobel ME. Decreased expression of galectin-3 is associated with progression of human breast cancer. J Pathol. 1996. 179:43-48.

5. Molecular diagnostics.

While at the NCI, my group trained scientists and pathology residents in molecular techniques to diagnose cancers. I collaborated with Maria Merino, Chief of Surgical Pathology at NCI. We utilized micro- and macro-dissection to examine loss of heterozygosity associated with carcinomas of the breast, ovary, thyroid, colon, and kidney. I also became a spokesperson for the ethical use of human biological samples in research. Since leaving the NIH, I have continued those efforts and have focused on the training and education of scientists and pathology residents in genomic medicine.

a. Sobel ME. Ethical issues in molecular pathology: paradigms in flux. Arch Pathol Lab Med. 1999. 123:1076-1078.
b. Schrijver I, Aziz N, Farkas DH, Furtado M, Ferreira Gonzalez A, Greiner TC, Grody WG, Hambuch T, Kalman L, Kant JA, Klein RD, Leonard DGB, Lubin IM, Mao, R, Nagan N, Pratt VM, Sobel ME, Voelkerding KV, Gibson JS. Opportunities and challenges associated with clinical diagnostic genome sequencing: a report of the Association for Molecular Pathology. J Mol Diagn. 2012. 14:525-540.
c. Sobel ME, Dreyfus JD. Disruptive influences on research in academic pathology departments: Proposed changes to the Common Rule governing informed consent for research use of biospecimens and to rules governing return of research results. Am J Pathol. 2017. 187:4-8.
d. Sobel ME, Dreyfus JC, Dillhay McKillip K, Kolarcik C, Muller WA, Scott MJ, Siegal GP, Wadosky K, O'Leary TJ. Return of individual research results: a guide for biomedical researchers utilizing human biospecimens. Am J Pathol. 2020. 190:918-933.

D. Research Support (no current support)