BIOGRAPHICAL SKETCH

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NAME: Schwarzbauer, Jean E.

eRA COMMONS USER NAME (credential, e.g., agency login): JESCHWARZBAUER

POSITION TITLE: Eugene Higgins Professor, Associate Chair of Molecular Biology

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Wisconsin, Milwaukee, WI	BS	05/1974	Chemistry
Univ. of Wisconsin Medical School, Milwaukee, WI	Graduate Student	05/1975	Pathology Grad. Prog.
University of Wisconsin, Madison, WI	PHD	05/1980	Molecular Biology
MIT Center for Cancer Research, Cambridge, MA	Postdoctoral Fellow	06/1986	Postdoctoral

A. Personal Statement

My lab has a longstanding interest in deciphering mechanisms that govern extracellular matrix (ECM) assembly, specifically the role of fibronectin in directing the assembly of a definitive matrix. Specific questions and scientific problems have evolved from an initial focus on the fibronectin molecule, its binding domains and alternative splicing, to our current focus on dissection of complex mechanistic issues related to the ECM. My group has established bacterial, insect, and mammalian cell expression systems to prepare large quantities of full-length recombinant fibronectin, fibronectin fragments, and other ECM proteins. We have combined these recombinant proteins with cell lines that allow us to control the initiation of fibril formation, to identify regions required for de novo assembly and fibril insolubility, and to determine intracellular pathways that regulate fibronectin matrix stability and integrin-matrix interactions. Microscopic, biochemical, and molecular approaches and, more recently, biophysics, engineering principles, and biomaterials strategies have been applied to address both old and emerging questions of ECM assembly and the role of this process in various tissue functions. Over the years, I have worked with collaborators who provide expertise that allows me to tackle new questions related to ECM. I have a demonstrated record of research productivity in ECM biology, including its relevance to developmental and disease processes. Furthermore, I am a proven leader in the cell biology and ECM biology scientific communities with service on numerous national and international boards, advisory panels, and within scientific society leadership.

Ongoing and recently completed projects that I would like to highlight include:

R01 AR073236-01
Schwarzbauer (PI)
5/1/18 - 4/30/24
Fibronectin-dependent mechanisms governing the assembly of a definitive extracellular matrix

Sud Cook ’39 Fund for the Prevention of Addiction to Alcohol and other Mind-altering Drugs
Schwarzbauer (PI)
10/1/17 – 9/30/23
Regulation of synaptic plasticity by the extracellular matrix

Citations:

1. Resnikoff HA, Miller CG, Schwarzbauer JE. Implications of fibrotic extracellular matrix in diabetic retinopathy. Exp Biol Med (Maywood). 2022;247:1093-1102. PubMed Central PMCID: PMC9335512.
2. Harris GM, Raitman I, Schwarzbauer JE. Cell-derived decellularized extracellular matrices. Methods Cell Biol. 2018;143:97-114. PubMed Central PMCID: PMC5995326.
3. Singh P, Carraher C, Schwarzbauer JE. Assembly of fibronectin extracellular matrix. Annu Rev Cell Dev Biol. 2010;26:397-419. PubMed Central PMCID: PMC3628685.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2021	NIH Arthritis, Connective Tissue, and Skin (ACTS) Study Section, ad hoc member
2019 - 24	Board of Scientific Counselors, National Heart, Lung, and Blood Institute (NHLBI)
2018	NIH Fellowship SEP – Cell Biology, Developmental Biology, Bioengineering
2017	NIH Director's Transformative Research Award Initiative review panel
2016	NIH Special Emphasis Panel, Program Project Grants – Cell Biology
2016	National Advisory General Medical Sciences Council, ad hoc member
2015	Expert Panelist, NIH workshop on Cell Line Authentication and Data Reproducibility
2014 - 17	HHMI Gilliam Fellowship review panel
2013 - 15	NIH Arthritis, Connective Tissue, and Skin (ACTS) Study Section, ad hoc member
2013	NIH Engineering, Cell, and Development Fellowship Study Section, ad hoc member
2013 -	Associate Editor, Matrix Biology
2013 -	Associate Chair of Molecular Biology, Princeton University
2011 -	Associate Member, Cancer Institute of New Jersey, New Brunswick, NJ
2011	NIH ICI Study Section, ad hoc member
2009 - 10	Program Chair, ASMB 2010 Biennial meeting
2009	Reviewer, U.S. Army CDMRP Breast Cancer Review panel
2008 - 13	Director of Graduate Studies for the Molecular Biology Program, Princeton
2008 - 09	NIH Oncology Fellowship study section, ad hoc reviewer
2007	NSF Advisory Workshop: Cell as a Machine
2005	Co-organizer, ASCB-ECI Engineering Cell Biology conference
2005 - 06	Chair, NIH Intercellular Interactions (ICI) Study Section (inaugural year)
2003 - 04	Chair, NIH Pathobiochemistry (PBC) Study Section (study section discontinued)
2003 - 19	NIH-COBRE Nebraska Center for Cellular Signaling External Advisory Board
2002	NIH/NIGMS "Visions of the Future" Workshop
2001 - 06	Editorial committee, Annual Review of Cell and Developmental Biology
2001 - 08	ASCB, Women in Cell Biology Committee (WICB)
1999 -	NIH Special Emphasis Panel reviewer or chair (1999, 2000, 2006, 2009, 2010, …)
2001 - 02	American Cancer Society grant review committee
2007 -	Editor, Molecular Biology of the Cell; Editorial Board, 2000 - 02; Associate Editor, 2003 - 06
2000 - 04	AHA National Research Committee
2001	NIH CDF4 Study Section temporary member
2001 -	Core faculty member, New Jersey Center for Biomaterials training program, Piscataway, NJ
2000 -	Professor of Molecular Biology, Princeton University, Princeton, NJ
2000	Program Chair – ASCB 40th Annual Meeting
1995 - 18	Editorial Board, Journal of Cell Biology
1993 - 00	Associate Professor of Molecular Biology, Princeton University, Princeton, NJ
1993 - 09	Associate Editor, Cell Communication and Adhesion
1994 - 99	NIH Pathobiochemistry Study Section permanent member.
1986 - 93	Assistant Professor of Molecular Biology, Princeton University, Princeton, NJ
1980 - 86	Postdoctoral Fellow with Dr. Richard Hynes, MIT Center for Cancer Research, Cambridge, MA

Honors

2019 - 25	International Society for Matrix Biology Council
2018	ASMB Senior Investigator Awardee
2017	ASCB Fellow
2016	Ruth Chiquet-Ehrismann Tribute Lecture, ASMB Biennial meeting

2015	Eugene Higgins Professor of Molecular Biology
2014	Princeton Dean for Research Innovation Award
2013	First recipient, Peggy Wheelock Award for Excellence in Research, Mentoring, and Promotion of Women in Science, Univ. of Nebraska Medical Center
2013	5-year renewal of our 25-slot NIH Predoctoral Training Grant in Genetics and Molecular Biology
2011	Keynote speaker, 50th Anniversary of CMB Grad Program, UW-Madison
2011 - 12	President of ASMB (President elect, 2009-2010; Past-President, 2013-2014)
2008 - 09	Elected to American Society for Matrix Biology (ASMB) Council
2006 - 11	Elected ASCB Secretary, two terms
2003 - 06	Elected to the American Society for Cell Biology (ASCB) Council
2001 - 07	Elected to Board of Trustees, Gordon Research Conferences
1993, 95	Vice Chair and Chair, Fibronectin, Integrins, and Related Molecules Gordon Conference
1987 - 92	American Heart Association Established Investigator
1984 - 86	Charles A. King Trust Postdoctoral Fellow
1980 - 82	Damon Runyon-Walter Winchell Postdoctoral Fellow
1973	NSF-Undergraduate Research Program Award

Memberships: ASCB, AAAS, ASMB, ASBMB, NAVBO, International Society for Matrix Biology

C. Contribution to Science

1. My earliest contribution to fibronectin biology was **the discovery that multiple fibronectin mRNAs arise from alternative splicing of a single gene transcript.** This was one of the first reports of alternative splicing of a normal cellular transcript; differential splicing had been reported for many viral transcripts. The initial finding identified a novel mechanism of splicing by exon subdivision to generate three different isoforms at the V region in rodents; two other domains (EIIIA and EIIIB) are spliced by exon skipping. V region-specific antibodies were used to demonstrate that this region is excluded from some subunits of plasma fibronectin, thus explaining the derivation of certain fibronectin isoforms. Many subsequent studies by myself and many other research groups have investigated functions of these spliced domains.

    a. Wilson CL, Schwarzbauer JE. The alternatively spliced V region contributes to the differential incorporation of plasma and cellular fibronectins into fibrin clots. J Cell Biol. 1992 Nov;119(4):923-33. PubMed Central PMCID: PMC2289702.

    b. Schwarzbauer JE, Spencer CS, Wilson CL. Selective secretion of alternatively spliced fibronectin variants. J Cell Biol. 1989 Dec;109(6 Pt 2):3445-53. PubMed Central PMCID: PMC2115891.

    c. Schwarzbauer JE, Paul JI, Hynes RO. On the origin of species of fibronectin. Proc Natl Acad Sci U S A. 1985 Mar;82(5):1424-8. PubMed Central PMCID: PMC397274.

    d. Schwarzbauer JE, Tamkun JW, Lemischka IR, Hynes RO. Three different fibronectin mRNAs arise by alternative splicing within the coding region. Cell. 1983 Dec;35(2 Pt 1):421-31. PubMed PMID: 6317187.

2. Fibronectin is a large dimeric protein with ~250 kDa subunits, numerous intramolecular disulfide bonds, and a pair of intermolecular disulfide bonds. Proper folding and dimerization requires **eukaryotic cell expression systems.** I first developed a novel murine retroviral vector for expression of truncated fibronectin dimers. This system was very useful for dissecting the functions and interactions of fibronectin domains including the V region, the C-terminal heparin binding domain, and domains involved in matrix assembly. For expression of full length fibronectin, recombinant tenascin-C, and other large ECM proteins, we established a baculovirus insect cell expression system. These proteins have been critical to determining matrix assembly and adhesion modulatory roles for these proteins.

    a. Sechler JL, Rao H, Cumiskey AM, Vega-Colón I, Smith MS, Murata T, Schwarzbauer JE. A novel fibronectin binding site required for fibronectin fibril growth during matrix assembly. J Cell Biol. 2001 Sep 3;154(5):1081-8. PubMed Central PMCID: PMC2196193.

    b. Wenk MB, Midwood KS, Schwarzbauer JE. Tenascin-C suppresses Rho activation. J Cell Biol. 2000 Aug 21;150(4):913-20. PubMed Central PMCID: PMC2175281.

c. Corbett SA, Lee L, Wilson CL, Schwarzbauer JE. Covalent cross-linking of fibronectin to fibrin is required for maximal cell adhesion to a fibronectin-fibrin matrix. J Biol Chem. 1997 Oct 3;272(40):24999-5005. PubMed PMID: 9312106.

d. Aguirre KM, McCormick RJ, Schwarzbauer JE. Fibronectin self-association is mediated by complementary sites within the amino-terminal one-third of the molecule. J Biol Chem. 1994 Nov 11;269(45):27863-8. PubMed PMID: 7961716.

3. My lab has made significant contributions to our **understanding of the step-wise mechanism of fibronectin matrix assembly.** Using full-length recombinant fibronectins with mutations or deletions, we have identified regions that control the rate of assembly, the organization of fibrils, and the conversion of fibrils into the insoluble form. These results are significant because fibronectin matrix provides an essential platform for deposition of many other matrix proteins so proper formation of the fibronectin matrix is critical for normal tissue development and homeostasis.

   a. Hill KE, Lovett BM, Schwarzbauer JE. Heparan sulfate is necessary for the early formation of nascent fibronectin and collagen I fibrils at matrix assembly sites. J Biol Chem. 2022 Jan;298(1):101479. PubMed Central PMCID: PMC8801470.

   b. Garrison CM, Schwarzbauer JE. Fibronectin fibril alignment is established upon initiation of extracellular matrix assembly. Mol Biol Cell. 2021 Apr 15;32(8):739-752. PubMed Central PMCID: PMC8108514.

   c. Saunders JT, Schwarzbauer JE. Fibronectin matrix as a scaffold for procollagen proteinase binding and collagen processing. Mol Biol Cell. 2019 Aug 1;30(17):2218-2226. PubMed Central PMCID: PMC6743462.

   d. Raitman I, Huang ML, Williams SA, Friedman B, Godula K, Schwarzbauer JE. Heparin-fibronectin interactions in the development of extracellular matrix insolubility. Matrix Biol. 2018 Apr;67:107-122. PubMed Central PMCID: PMC5910196.

4. We have applied our knowledge of cell-ECM interactions to the **development of novel materials with potential for use in tissue engineering and implant devices.** Through collaborations, we have studied the effects of nanoparticles, topology, surface modification, and patterning on cell behavior and extracellular matrix assembly. In particular, my collaboration with Jeffrey Schwartz (Chemistry, Princeton University) has been particularly fruitful. Our studies have evolved from peptide-functionalized chemical interfaces for selective cell attachment to metals to our most recent, and most exciting, work directing the organization of cell-assembled matrix using patterned chemical interfaces on soft polymeric materials. We showed that linear arrays of fibronectin fibrils will direct the oriented extension of neurites and we are currently developing materials to test in implant studies for nervous system repair.

   a. Sharma A, Schwarzbauer JE. Differential regulation of neurite outgrowth and growth cone morphology by 3D fibronectin and fibronectin-collagen extracellular matrices. Mol Neurobiol. 2022 Feb;59(2):1112-1123. PubMed Central PMCID: PMC8858852.

   b. Garrison CM, Singh-Varma A, Pastino AK, Steele JAM, Kohn J, Murthy NS, Schwarzbauer JE. A multilayered scaffold for regeneration of smooth muscle and connective tissue layers. J Biomed Mater Res A. 2021 May;109(5):733-744. PubMed Central PMCID: PMC7855544.

   c. Harris GM, Madigan NN, Lancaster KZ, Enquist LW, Windebank AJ, Schwartz J, Schwarzbauer JE. Nerve Guidance by a Decellularized Fibroblast Extracellular Matrix. Matrix Biol. 2017 Jul;60-61:176-189. PubMed Central PMCID: PMC5352540.

   d. Singh S, Bandini SB, Donnelly PE, Schwartz J, Schwarzbauer JE. A cell-assembled, spatially aligned extracellular matrix to promote directed tissue development. J Mater Chem B. 2014 Mar 21;2(11):1449-1453. PubMed Central PMCID: PMC3975264.

5. Throughout my career, as I learned more about fibronectin and how it is organized into a fibrillar matrix, I have **investigated the role of the ECM in a variety of biological processes.** We have studied processes in development (such as chondrogenesis, amphibian gastrulation and C. elegans gonad morphogenesis), basic cellular processes including cell contractility and signaling, and disease models such as tumor formation, skeletal defects, and fibrosis. The results of these studies have shown the

importance of the ECM in normal cellular functions and in disease and have suggested new mechanisms that we are continuing to pursue.

a. Cadoff EB, Sheffer R, Wientroub S, Ovadia D, Meiner V, Schwarzbauer JE. Mechanistic insights into the cellular effects of a novel FN1 variant associated with a spondylometaphyseal dysplasia. Clin Genet. 2018 Nov;94(5):429-437. PubMed Central PMCID: PMC6175647.

b. Singh P, Schwarzbauer JE. Fibronectin matrix assembly is essential for cell condensation during chondrogenesis. J Cell Sci. 2014 Oct 15;127(Pt 20):4420-8. PubMed Central PMCID: PMC4197087.

c. Miller CG, Pozzi A, Zent R, Schwarzbauer JE. Effects of high glucose on integrin activity and fibronectin matrix assembly by mesangial cells. Mol Biol Cell. 2014 Aug 15;25(16):2342-50. PubMed Central PMCID: PMC4142608.

d. Meighan CM, Schwarzbauer JE. Control of C. elegans hermaphrodite gonad size and shape by vab-3/Pax6-mediated regulation of integrin receptors. Genes Dev. 2007 Jul 1;21(13):1615-20. PubMed Central PMCID: PMC1899471.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/jean.schwarzbauer.1/bibliography/public/