BIOGRAPHICAL SKETCH

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NAME Joseph Michael Chalovich	POSITION TITI Professor	POSITION TITLE Professor		
eRA COMMONS USER NAME chalovichj				
EDUCATION/TRAINING (Begin with baccalaureate or other initial	professional education,	such as nursing, and	d include postdoctoral training.)	
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY	
Pennsylvania State University, Univ. Park	B.S.	1974	Biochemistry	
Virginia Polytechnic Institute & State Univ.,	M.S.	1976	Biochemistry & Nutrition	

Ph.D.

1978

Biochemistry

University of Illinois Medical Center, Chicago

A. POSITIONS AND HONORS

Positions and Employment

1978-1979:	Research Associate with Dr. Michael Bárány, University of Illinois Medical Center.
1979-1984:	Staff Fellow with Dr. Even Eisenberg, National Institutes of Health.
1984-1989:	Assistant Professor, Dept. of Biochemistry, East Carolina Univ. Medical School
1989-1992:	Associate Professor, Dept. of Biochemistry, East Carolina Univ. Medical School
1992-2005:	Professor, Department of Biochemistry, East Carolina Univ. School of Medicine
2005-present:	Distinguished Research Professor of Biochemistry & Molecular Biology, ECU
2014-2016:	Interim Chairman, Department of Biochemistry & Molecular Biology, ECU

Other Experience

Blacksburg

Co-Chair, Biophysical Society Motility Subgroup (1991-92) Editorial Board: J. Muscle Research and Cell Motility, 1992-Ad Hoc Member NIH Physiology Study Section (1992) Research Committee, N.C. Affiliate American Heart Association (1993-95) Research Committee member, N.C. Affiliate American Heart Association (1993-1995) Ad Hoc Member NIH Biophysical Chemistry Study Section (1993) Member NIH Biophysical Chemistry Study Section (1995-1999) Regular Ad Hoc Reviewer for NIH Grant Reviewer for the Welcome Trust Grant Reviewer for the Israel Science Foundation Director of the Motility and Cytoskeleton Research Interest Group at the Brody School of Medicine Visiting Professor University of Ulm (Germany) Visiting Professor University of Hannover (Germany)

<u>Honors</u>

1976: Phi Sigma Award

1977: Sigma Xi Certificate of Recognition

1978: Sigma Xi Certificate of Recognition

2004: Faculty Helms Award for Research, East Carolina University Society of Sigma Xi

2005: Lifetime Achievement Award for Excellence in Research & Creative Activity (from ECU)

2005: Founding Charter Member Award, Greenville Community Shelters

2005: President East Carolina Chapter of Sigma Xi.

2017 Mission Champion, Brody School of Medicine at East Carolina University

2017 University Scholar; East Carolina University

B. PEER-REVIEWED PUBLICATIONS

- Chalovich, J.M., Burt, C.T., Cohen, S.M., Glonek, T., and Barany, M. (1977) Identification of an unknown 32P nuclear magnetic resonance from dystrophic chicken as L-serine ethanolamine phosphodiester. Arch. Bioch. Biophys. 182, 683-689.
- Burt, C.T., and Chalovich, J.M. (1978) A major phosphate component in chicken semen: serine ethanolamine phosphate. Biochem. Biophys. Acta. 529, 186-188. URL: <u>http://www.ncbi.nlm.nih.gov/pubmed/638178</u>
- 3. Chalovich, J.M., Burt, C.T., Danon, M.J., Glonek, T., and Barany, M. (1978) Phosphodiesters in muscular dystrophies. Ann. N.Y. Acad. Sci. 317, 649-669.
- Burt, C.T., Chalovich, J.M., Danon, M.J., Glonek, T., and Barany, M. (1978) Phosphorus nuclear magnetic resonance of diseased muscle. In Frontiers of Biological Energetics: Electrons to Tissues, P.L. Dutton, J.S. Leigh, and A. Scarpa (Eds.), New York, Academic Press, pp. 1371-1378.
- Chalovich, J.M., and Barany, M. (1980) Serine ethanolamine phosphate in avian muscular dystrophy: mechanism of accumulation in dystrophic muscle and relationship to phospholipid synthesis. Arch. Bioch. Biophys. 199, 615-625.
- Doyle, D.D., Chalovich, J.M., and Barany, M. (1981) Natural abundance ¹³C nmr spectra of intact muscle. FEBS lett. 131, 147-150. <u>PM:7286237</u>
- Chalovich, J.M., Chock, P.B., and Eisenberg, E. (1981) Mechanism of action of troponin-tropomyosin. Inhibition of actomyosin ATPase activity without inhibition of myosin binding to actin. J. Biol. Chem. 256, 575-578. <u>PM:6450206</u>
- Hill, T.L., Eisenberg, E., and Chalovich, J.M. (1981) Theoretical models for cooperative steady-state ATPase activity of myosin subfragment-1 on regulated actin. Biophys. J. 35, 99-112. DOI: 10.1016/S0006-3495(81)84777-7
- Chalovich, J.M. and Eisenberg, E. (1982) Inhibition of actomyosin ATPase activity by troponintropomyosin without blocking the binding of myosin to actin. J. Biol. Chem. 257, 2432-2437. <u>PM:6460759</u>
- Brenner, B., Schoenberg, M., Chalovich, J.M., Greene, L.E., and Eisenberg, E. (1982) Possible crossbridge attachment in relaxed muscle at low ionic strength. Proc. Natl. Acad. Sci. USA 79, 7288-7291. <u>PM:6961408</u>
- Barany, M., Chalovich, J.M., Burt, C.T., and Glonek, T. (1982) Nuclear magnetic resonance studies of muscle. In Disorders of the Motor Unit, D.L. Schotland (Ed.), New York, John Wiley and Sons, Inc., pp. 697-714.
- Chalovich, J.M., Greene, L.E., and Eisenberg, E. (1983) Crosslinked myosin subfragment-1: a stable analogue of the ATP complex of subfragment-1. Proc. Natl. Acad. Sci. USA 80, 4909-4913.
 <u>PM:6576363</u>
- Schoenberg, M., Brenner, B., Chalovich, J., Greene, L., and Eisenberg, E. (1984) Crossbridge attachment in relaxed muscle. In Crossbridge Mechanisms in Muscle Contraction, H. Sugi and G. H. Pollack (Eds.), New York, Plenum Corp., pp. 269-284.
- Chalovich, J. M., Chantler, P.D., Szent-Gyorgyi, A.G., and Eisenberg, E. (1984) Regulation of molluscan actomyosin ATPase by Ca²⁺. J. Biol. Chem. 259, 2617-2621.
- 15. Chalovich, J.M., Stein, L.A., Greene, L.E., and Eisenberg, E. (1984) Interaction of isozymes of myosin subfragment-1 with actin: effect of ionic strength and nucleotide. Biochemistry 23, 4885-4889.
- 16. Chalovich, J.M., and Fischetti, V.A. (1986) Crosslinking of actin filaments and inhibition of actomyosin subfragment-1 ATPase activity by streptococcal M6 protein. Arch. Biochem. Biophys. 245, 37-43.
- 17. Chalovich, J.M., and Eisenberg, E. (1986) The effect of troponin-tropomyosin on the binding of heavy meromyosin to actin in the presence of ATP. J. Biol. Chem. 261, 5088-5093.
- 18. Greene, L.E., Chalovich, J.M., and Eisenberg, E. (1986) Effect of nucleotide on the binding of N,N'-ρphenylenedimaleimide-modified S-1 to unregulated and regulated actin. Biochemistry 25, 704-709.
- Brenner, B., Chalovich, J.M., Greene, L.E., Eisenberg, E., and Schoenberg, M. (1986) Stiffness of skinned rabbit psoas fibers in MgATP and MgPPi solution. Biophys. J. 50, 685-691. DOI: 10.1016/S0006-3495(86)83509-3
- Chalovich, J.M., Cornelius, P., and Benson, C.B. (1987) Caldesmon inhibits skeletal actomyosin subfragment-1 ATPase activity of the binding of myosin subfragment-1 to actin. J. Biol. Chem. 262, 5711-5716.

- 21. Chalovich, J.M. (1988) Caldesmon and thin filament regulation of muscle contraction. Cell Biophys. 12, 73-86.
- 22. Hemric, M.E., and Chalovich, J.M. (1988) Effect of caldesmon on smooth and skeletal heavy meromyosin ATP hydrolysis and binding to actin. J. Biol. Chem. 263, 1878-1885.
- 23. Velaz, L., Hemric, M.E., Benson, C., and Chalovich, J.M. (1989) The binding of caldesmon to actin and its effect on the ATPase activity of soluble myosin subfragments in the presence and absence of tropomyosin. J. Biol. Chem. 264, 9602-9610.
- 24. Chalovich, J.M., Hemric, M.E., and Velaz, L. (1990) Regulation of ATP hydrolysis by caldesmon: a novel change in the interaction of myosin with actin. Ann. N.Y. Acad. Sci. 599, 85-99.
- 25. Velaz, L., Ingraham, R.H., and Chalovich, J.M. (1990) Dissociation of the effect of caldesmon on the ATPase activity and on the binding of smooth heavy meromyosin to actin by partial digestion of caldesmon. J. Biol. Chem. 265, 2929-2934.
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- 27. Hemric, M.E., and Chalovich, J.M. (1990) Characterization of caldesmon binding to myosin. J. Biol. Chem. 265, 19672-19678.
- 28. Brenner, B., Yu, Leepo, C., and Chalovich, J.M. (1990) Parallel inhibition of active force and relaxed fiber stiffness in skeletal muscle by caldesmon: Implications for the pathway to force generation. Proc. Natl. Acad. Sci. USA, 88, 5739-5743.
- 29. Chalovich, J.M., Yu, L.C., Velaz, L., Kraft, K. and Brenner, B. (1991) Caldesmon derived polypeptides as probes of force production in skeletal muscle. In Peptide Competition Approaches in Muscle Research, Springer Verlag, Heidelberg, J.C. Ruegg, ed.
- Stein, L.A., and Chalovich, J.M. (1991) Activation of skeletal S-1 ATPase activity by actin-tropomyosintroponin: Effect of Ca⁺⁺ on the fluorescence transient. Biophys. J 60, 399-407. DOI: 10.1016/S0006-3495(91)82065-3
- 31. Wang, C.-L. A., Chalovich, J.M., Graceffa, P., Lu, R.C., Mabuchi, K., and Stafford, W.F. (1991) A long helix from the central region of smooth muscle caldesmon. J.Biol.Chem. 266, 13958-13963.
- 32. Chalovich, J.M., Yu, L.C., and Brenner, B. (1991) Involvement of weak binding cross-bridges in force production in muscle. J. Muscle Res. Cell Motil. 12, 503-506.
- 33. Crosbie, R., Adams, S., Chalovich, J.M. and Reisler, E. (1991) The interaction of caldesmon with the COOH terminus of actin. J.Biol.Chem. 266, 20001-20006.
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- 45. Stafford, W.F., Chalovich, J.M., and Graceffa, P. (1994) Turkey gizzard caldesmon molecular weight and shape. Arch. Biochem. Biophys. 313, 47-49. DOI: 10.1006/abbi.1994.1356
- 46. Brenner, B., Chalovich, J.M., and Yu, L.C. (1995) Distinct molecular processes associated with isometric force generation and rapid tension recovery after quick release Biophys. J. 68, 106s-111s.
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- 48. Kraft, Th., Chalovich, J.M., Yu, L.C. and Brenner, B. (1995) Parallel inhibition of active force and relaxed fiber stiffness by caldesmon fragments at physiological ionic strength and temperature conditions. Biophys. J. 68,2404-2418. DOI: 10.1016/S0006-3495(95)80423-6
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- 56. Frisbie, S.M., Xu, S., Chalovich, J.M., and Yu, L.C. (1998) Characterizations of cross-bridges in the presence of saturating concentrations of MgAMP-PNP in rabbit permeabilized psoas muscle. Biophys J. 74, 3072-3082. DOI: 10.1016/S0006-3495(98)78014-2
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- Frisbie, M. C. Reedy, L. C. Yu, B. Brenner, J. M. Chalovich, and T. Kraft. (1999) Sarcomeric binding pattern of exogenously added intact caldesmon and its C-terminal 20-kDa fragment in skinned fibers of skeletal muscle. J.Muscle Res.Cell Motil. 20, 291-303.
- 61. B. D. Leinweber, R. S. Fredricksen, D. R. Hoffman, and J. M. Chalovich. (1999) Fesselin: a novel synaptopodin-like actin binding protein from muscle tissue. J.Muscle Res.Cell Motil. 20, 539-545.
- 62. B. Brenner, T. Kraft, L. C. Yu, and J. M. Chalovich. (1999) Thin filament activation probed by fluorescence of N-((2-(iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenz-2-oxa-1,3-diazole-labeled

troponin I incorporated into skinned fibers of rabbit psoas muscle. Biophys. J. 77, 2677-2691. DOI: 10.1016/S0006-3495(99)77102-X

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- Chen, Y.-D., Bo, Y., Chalovich, J.M. and Brenner, B. (2001) Theoretical kinetic studies of models for binding myosin subfragment-1 to regulated actin: Hill model vs. Geeves model. Biophys. J. 80: 2338-2349.
- 67. Sen, A., Chen, Y.-D., Bo, Y. and Chalovich, J.M. (2001) Caldesmon reduces the apparent rate of binding of myosin S1 to actin-tropomyosin. Biochemistry 40: 5757-5764.
- 68. Beall, B. and Chalovich, J.M. (2001) Fesselin, a synaptopodin-like protein, stimulates actin nucleation and polymerization. Biochemistry 40: 14252-14259. <u>PM:11714279</u>
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- 74. Schroeter, M. and Chalovich, J.M. (2004) Ca⁺⁺-Calmodulin Regulates Fesselin induced Actin Polymerization. Biochemistry 43: 13875-13882. DOI: 10.1021/bi0487490
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Letters, Reviews, and Book Chapters

- 1. Chalovich, J.M. (1983) Muscles of Mussels (and other creatures). Anal. Biochem. 130, 537 (Book Review)
- 2. Chalovich, J.M. (1990) Muscle contraction: muscle fiber studies support solution data. TIBS 15, 261.
- 3. Chalovich, J.M. (1992) Actin Filament Based Regulation of Motility. In Pharmacology and Therapeutics 55, 95-148.
- Chalovich, J.M. and Pfitzer, G. (1997) Structure and Function of the Thin Filament Proteins of Smooth Muscle. in: Cellular Aspects of Smooth Muscle Function; Cambridge University Press. Edited by C.Y. Kao and Mary E. Carsten. New York, NY
- 5. Chalovich, J.M. (2002) Regulation of striated muscle contraction: a discussion. J. Muscle Res. Cell Motil. 23:353-361. DOI: 10.1021/bi0273009
- 6. Chalovich, J.M., B.Yan, B.Brenner, and Y.D.Chen. 2002. Modeling thin filament cooperativity Response. Biophys J 82:1679-1681
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- 9. Chalovich, J.M. (2012) Disease causing mutations of troponin alter regulated actin state distributions. J. Muscle Res. Cell Motil.33: 493-9. DOI: 10.1007/s10974-012-9305-x
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- 11. Chalovich, J.M. and Johnson, D. (2016) Commentary: Effect of Skeletal Muscle Native Tropomyosin on the Interaction of Amoeba Actin with Heavy Meromyosin. Front. Physiol. 7: 377.
- 12. Chalovich, J.M., Kraft, T. and Yu, L.C. (2017) Obituary Bernhard Brenner. J Muscle Res Cell Motil. 38: 269-270.

History of Medicine lectures on video:

1.Franklinization: Early Therapeutic use of Static Electricity (2012) https://www.youtube.com/results?search_query=chalovich+franklinization 2.Nikola Tesla: How the vision for low cost energy led to fluorescent lights, radio and medical wonders. April 7, 2014 <u>https://www.youtube.com/watch?v=QnIFLDNkyfw</u>

Interview

https://www.youtube.com/watch?v=ofu7CJ_pm4s

https://www.reflector.com/news/ecu-researchers-find-potential-way-to-improve-activity-of-heartskeletal-muscles/article 22259408-2f90-5738-8028-b256667e9f63.html

Graduate Students Directed:

Mark E. Hemric, Ph.D. (1990) A Catalytically Inactive Actin-Caldesmon-Myosin Complex
Laly Velaz, Ph.D. (1991) Regulation of the Interaction Between Myosin and Actin by Caldesmon and its Subragments
Frank Lu, Ph.D. (1995) Caldesmon and Calponin Effects of the Myosin-Actin Interactions

Anindita Sen, Ph.D. (1997) The Role of the Competition between Caldesmon and Myosin-S1 in the Regulation of Actomyosin Interactions

Brent Beall, Ph.D. (2002) The Effects of Fesselin, A Synaptopo-Like Protien, nnc

Svetlana Hamden, Ph.D. (2008) Fesselin and Caldesmon: Natively Unfolded Proteins

Mohit Mathur, Ph.D. (2009) The Distribution f Regulated Actomyosin States Is Central to Cardiac Muscle Regulation and Disturbance of This Distribution Leads to Congeital Cardiomyopathies

Nathanial Kingsbury, M.S. (2015) Fessselin, an intrinsically disordered smooth muscle protein, organizes and stabilizes actin-myosin and myosin.

Dylan Johnson, M.S. (2016), PhD

Foreign Graduate Research done, in part, in the Chalovich lab

Susanne Schnekenbühl (1992) Kalzium-unabhaengige Aktivierung membranfrier Muskelpräparate. Ist die Muskelkontraktion ueber zwei verschiedene Mechanismen reguliert? Stefan Heizmann (1995) Untersuchungen zur Function des glattmuskuläeren Regulatorproteins Calponin. Elke Thedinga (1997) Charakterisierung von Myosin – Isoformen mit dem *in vitro* Motility Assay.

Representative Committee Assignments

Chairman Personnel Committee Biochemistry & Molecular Biology Co-chair of Research Review for Mission Based Management Co-Chair of Research Infrastructure Assessment Team (RIAT) Brody SOM (2007-2008) East Carolina University Master Plan Committee (2009-2010) Chancellors Research Advisory Committee (2005) Review of ECU Department of Chemistry Brody School of Medicine Representative to EDGE Magazine Research Committee, Brody School of Medicine Radiation Safety Committee Sustainability Committee (2015- 2017) Brody Council (2015-2017) Interim Chair Department of Biochemistry & Molecular Biology (2014-2016)

Courses Taught

Chemistry 2770; (course director) Medical Biochemistry (7300) Biochemistry I (BIOC 7301) Introduction to Research (BIOC 7330) Seminar in Biochemistry (BIOC 7335; course director) Cell Motility (BIOC 7345; course director) Current Topics (BIOC 7355) Physical Biochemistry (8305, course director) Dental Biochemistry, (section director) Introduction to Medical Biochemistry (Summer Class) Problem Based Learning 1st and 2nd year medical students

C. RESEARCH SUPPORT

Principle and Sole Investigator (Total funding as single P.I. >3.4 million)

Actin Based Regulation of Smooth Muscle Contraction

National Institutes of Health R01-AR35216

This grant was funded for 22 years (1985-2007). During that time, it provided 25% of my salary, supported graduate students, medical students, postdoctoral fellows and technicians. That grant provided up to \$80,000/year overhead.

That project determined the mechanisms of action of caldesmon and calponin in the regulation of smooth muscle contraction. That work also led to the discovery of the protein fesselin (synaptopodin 2), an important unstructured protein that controls the assembly of actin and myosin and is involved in some types of cancer.

Protein Exchange to Study Muscle function and Disease

National Institutes of HealthR01- AR44505

That grant was funded for 11 years (1997-2008) and covered 25% of my salary. This grant explores the mechanism of familial hypertrophic cardiomyopathy that results from mutations in troponin I and troponin T. The hypothesis tested is that mutations shift the ratio of active and inactive states of actin away from the normal distribution. Familial hypertrophic cardiomyopathy is an example of a disorder that generally stabilizes the active state whereas dilated cardiomyopathy tends to stabilize the inactive state.

We studied changes in the regulation of ATPase activity caused by mutants of troponin that cause Familial Hypertrophic Cardiomyopathy. Together with my collaborator in Germany, we showed that observations made with soluble proteins held true in single muscle fibers.

Role of Weakly Bound Crossbridges in Muscle Contraction

National Institutes of Health R01-AR40540

That grant was funded for 5 years (1990-1995) and covered 25% of my salary. We showed that myosin does bind to actin even in relaxed muscle. We showed that muscle contraction required the formation of low affinity attachments between myosin and actin prior to force generation. That grant was an important step in developing the techniques required to study cardiac disorders.

Other grants were obtained from the American Heart Association and NATO.

Co-Principle Investigator:

Role of Synaptopodin 2 in Cancer

Brody Brothers Endowment Fund (Chalovich, J.M. & Schroeter, M.M. P.I.'s)

This local exploratory grant was funded for 1 year. This grant allowed us to prepare unique custom antibodies that are now being used to study changes in the cellular distribution of synaptopodin isoforms in cancer. We are about to publish a paper that shows that synaptopodin 2 enters the nucleoli of some cells.

Regulatory mechanism of Contraction in Skeletal Muscle

NATO Collaborative Research Grant CRG 900257 (Yu, L.C., Brenner, B., and Chalovich, J.M. co-Pl's.

That grant provided funds for travel among our laboratories in Greenville, NC, Washington, DC Ulm Germany and Hannover Germany. This enabled us to combine biochemical, physiological and physical approaches to the study of muscle contraction.

Deciphering the function of the COOH region of troponin T in normal cardiac function and in Hypertrophic cardiomyopathy.

Brody Brothers Endowment Fund (Chalovich, J.M. & Burns, C. P.I.'s)

The purpose of this 1-year grant was to determine the effect of the 14-C-terminal residues of cardiac troponin on the distribution of actin-tropomyosin-troponin among its regulatory states.

Awards to support students and fellows

5 American Heart Association grants to support 4 graduate students and 1 postdoctoral fellow. NIH National Research Service Award (F32HL090206) awarded to Dr. Mohit Mathur to cover the expenses of his Ph.D. degree.

Howard Hughes student fellowship to Dr. Robert Oxford (MD student):

D. GREENVILLE COMMUNITY WORK:

Founding Charter Member of Greenville Community Shelters First Secretary/Treasurer of Greenville Community Shelters Vice President Greenville Community Shelters Volunteer Night Guard Greenville Community Shelters Volunteer Food Server Greenville Community Shelters Capital Campaign Fundraiser for the Catholic Diocese of Raleigh St. Gabriel's Church parish council St. Gabriel's Church finance committee St. Gabriel's Church construction committee St. Gabriel's Church maintenance committee St. Gabriel's Church social action committee. (member for 20 years, 15 as chairman) Hurricane Floyd Red Cross volunteer Habit for Humanity volunteer Pioneer Days: electricity demonstrations Boys & Girls Club Health Days: electricity demonstrations at 5 annual events Board of Trustees for John Paul II High School (2015-) Ulster Project: Directed Irish and American Teens in building picnic tables and benches for A TIME FOR SCIENCE Board of Trustees for John Paul II High School (2014-) Chairman of Recruitment Committee for John Paul II High School (2014-) Member of Executive Fundraising Committee for John Paul II High School (2015-) Chairman of the Board of Trustees for John Paul II High School (2016-). Volunteer for CareNet, The Baptist Mental Health Facility (2018-)

Annual Demonstrations of high voltage electricity for A Time For Science (2013-)