THE BIOLOGY OF CALPAINS IN HEALTH AND DISEASE

JULY 21-26, 2013 SAXTONS RIVER, VT

CO-ORGANIZERS:

Jim Geddes University of Kentucky Lexington, KY

Peter Greer Queen's University Kingston, ON, Canada





Federation of American Societies for Experimental Biology

SRC: Science Research Conferences

The Biology of Calpains in Health and Disease

July 21-26 Saxtons River, Vermont

Co-Organizers:

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Advisory Committee:

Peter Davies, Queens University, Canada Anna Huttenlocher, University of Wisconsen Jun Inoue, Senju Pharmaceuticals, Japan Mohammad Koohmaraie, IEH Laboratories Graham Lamb, La Trobe Univ., Australia Masatoshi Maki, Nagoya University, Japan Ronald Mellgren, University of Toledo David Park, University of Ottawa, Canada Taikomi Saido, Riken Brain Science Institute, Japan Hiroyuki Sorimachi, Tokyo Metropolitan Institute of Medical Science Melissa Spencer, Univ., California, Los Angeles Kevin Wang, University of Florida



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Biology of Calpains in Health and Disease July 21-26, 2013 Saxtons River, Vermont

Co-Organizers: Jim Geddes University of Kentucky

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Sunday,

4:00PM – 9:00PM	Conference Registration
6:00PM – 7:00PM	FASEB Opening Reception
7:00PM – 8:30PM	Dinner
8:45PM – 9:00PM	Welcoming Remarks Jim Geddes and Peter Greer
9:00PM – 10:00PM	Keynote Lecture : Peter Davies, Queen's University "What have we learned about calpains from structural biology?"

Monday, July 22, 2013 7:30AM – 9:00AM	Breakfast
Session 1: 9:00AM – 12:15PM	Bioinformatics of Calpain Substrates Session co-Chairs: Hiroyuki Sorimachi, Tokyo Metropolitan Institute of Medical Science Hiroshi Mamitsuka, Bioinformatics Center, Kyoto University
9:00AM – 9:15AM	Welcome from FASEB
9:15AM – 9:45PM	Dorothy Croall, University of Maine "A brief history of calpains"
9:45AM – 10:15AM	Daniel MacQueen, University of Aberdeen "Molecular Evolution of Calpains"
10:15AM – 10:45AM	Group photo & FASEB Sponsored Coffee Break
10:45AM - 11:15AM	Hiroshi Mamitsuka, Bioinformatics Center, Kyoto University "Basics of machine learning and bioinformatics"
11:15AM –11:45AM	David DuVerle, Advanced Industrial Science and Technology "Predicting calpain cleavage with machine-learning techniques"
11:45AM – 12:00 PM	Fumiko Ouchi, Tokyo Metropolitan Institute of Medical Science "Towards understanding the 'substrate specificity' of calpain by proteomics and bioinformatics"
12:00PM – 12:15PM	Hiroyuki Sorimachi and Peter Davies "Calpain nomenclature: Introduction"
12:15PM – 1:15PM	Lunch
	Free Afternoon
4:00PM - 6:00PM	Poster Session 1
6:00PM – 7:00PM	Dinner
Session 2: 7:00PM – 9:45PM	Calpains and Cancer Session Chair Peter Greer, Queen's University
7:00PM - 7:30PM	Stewart Martin, University of Nottingham "The calpain system and cancer"

7:30PM – 8:00PM	Maralice Conacci-Sorrell*, Fred Hutchinson Cancer Research Center " <i>Calpain-induced Myc-nick in colon cancer</i> "
8:00PM – 8:15PM	Stacy Visser-Grieve, Queen's University "Calpain mediates sensitivity to targeted therapeutics in breast cancer cells"
8:15PM – 8:30PM	Break
8:30PM – 8:45PM	Vinit B. Mahajan, Columbia University <i>"Calpain-5 retinopathy in mice using a human CAPN5-</i> <i>R243L lentiviral vector"</i>
8:45PM – 9:15PM	Alan Wells, University of Pittsburgh "Calpains as potential anti-cancer targets"
9:15PM – 9:45PM	Peter Greer, Queen's University "Calpain 2 regulates Akt-FoxO-p27(Kip1) protein signaling pathway in mammary carcinoma"

Tuesday,

July 23, 2013 7:30AM – 9:00AM	Breakfast
Session 3 9:00AM – 12:15PM	Measuring Calpain Activation Session Chair: Kevin Wang, University of Florida
9:00AM – 9:30AM	Kevin Wang, University of Florida "Calpain substrates as biomarkers for neuro-injury and neuro- diseases"
9:30AM – 10:00AM	John Anagli, Banyan Biomarkers "Absolute quantitation of neuronal-glial injury biomarkers"
10:00AM – 10:15AM	Maemoto Yuki, Nagoya Univ. "Analyses of ESCRT-dependent limited proteolytic activities of calpain-7 in mammalian cells"
10:15AM – 10:45AM	FASEB Sponsored Coffee Break
10:45AM – 11:15AM	Hiroyuki Sorimachi, Tokyo Metropolitan Institute of Medical Science "Extended concept for calpain "activity" – non-proteolytic functions of unconventional calpains"
11:15AM – 11:30AM	Jeannette Hübener, University of Tübingen "Strategies for analyzing calpain-mediated ataxin-3 cleavage in the molecular pathogenesis of SCA3"

11:30AM – 12:15PM	Hiroyuki Sorimachi and Peter Davies "Calpain nomenclature: Discussion"
12:15PM – 1:15PM	Lunch
1:15PM – 6:00PM	Free Afternoon
6:00PM – 7:00PM	Dinner
Session 4: 7:00PM – 9:45PM	Calpain in Cell Death Pathways Session Chair: Jim Geddes, University of Kentucky
7:00PM – 7:30PM	Jinsoo Seo, Picower Institute For Learning and Memory, MIT "Calpain-resistant p35 reveals the role of p25/Cdk5 in synaptic plasticity and neurodegeneration in vivo"
7:30PM – 8:00PM	Tetsumori Yamashima, Kanazawa University Graduate School of Medicine "Why are hippocampal CA1 neurons so vulnerable to transient ischemia?"
8:00PM – 8:15PM	Nechama Kosower, Tel-Aviv University "Mycoplasma and lipid-containing agonists for Toll-Like Receptor 2 (TLR2) upregulate calpastatin: possible treatment of calpain-related disorders"
8:15PM – 8:30PM	Break
8:15PM – 8:30PM	Christopher Norris, University of Kentucky "Calpain interactions with the protein phosphatase calcineurin in Alzheimer's disease"
8:45PM – 9:15PM	Fumihiko Urano, U. Mass. Medical School "m-calpain induces neuronal and beta cell death in Wolfram syndrome"
9:15PM – 9:45PM	Jim Geddes, University of Kentucky "Calpain 5: An atypical calpain enriched in the brain and spinal cord"

Wednesday,

July 24, 2013 7:30AM – 9:00AM	Breakfast
Session 5 9:00AM – 12:15PM	Calpains in Diabetes and Other Disorders Session Chair: Athar Chishti, Tufts University
9:00AM - 9:30AM	Ingrid Fleming, Goethe-Universität, "The role of calpain in diabetes-associated platelet hyperactivation"
9:30AM –10:00AM	Rosario Scalia, Temple University <i>"Calpain and regulation of endothelial function in obesity with insulin resistance"</i>
10:00AM – 10:30AM	Yi-Shiuan Huang, Inst. Biomedical Sciences, Academia Sinica <i>"Calpain 2 activated through the NMDA receptor signaling cleaves</i> <i>CPEB3"</i>
10:30AM – 11:00AM	FASEB Sponsored Coffee Break
11:00AM – 11:30AM	Athar Chishti, Tufts University "Calpain 1 and sickle cell disease"
11:30AM – 12:00PM	Adam Goldfarb, University of Virginia "Calpain-2 promotes megakaropoesis through activation of Cdk9"
12:00PM – 12:15PM	Peter R. Hoffmann, University of Hawaii "Calpastatin prevents NF-кВ mediated hyperactivation of macrophages and attenuates colitis"
12:15PM – 1:15PM	Lunch
	Free Afternoon
4:00PM - 6:00PM	Poster Session 2
6:00PM – 7:00PM	Dinner
Session 6: 7:00PM – 9:45PM	Calpains in Neurodegeneration Session Chair: David Park, University of Ottawa
7:00PM - 7:30PM	Takaomi Saido, RIKEN Brain Science Institute "The role of calpain-calpastatin system in a single-locus knockin mouse model of AD"
7:30PM – 8:00PM	Shin Kwak, University of Tokyo "Calpain cleavage of TDP-43 in amyotrophic lateral sclerosis"

8:00PM – 8:15PM	Break
8:15PM – 8:45PM	Yoshiyuki Tamada, Senju Pharmaceutical Co. "Calpain in retinal neuropathies due to ischemia"
8:45PM – 9:15PM	Michel Baudry, Western University of Health Sciences "Novel roles of calpains in synaptic plasticity and neurodegeneration"
9:15PM – 9:45PM	Kathryn Saatman, University of Kentucky "Calpain as a therapeutic target in traumatic brain injury"
Thursday, July 25, 2013	Breakfast
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Session 7 9:00AM – 12:15PM	Calpains in Cardiovascular Diseases Session Chair: Kinya Otsu, King's College
9:00AM – 9:30AM	Tianqing Peng, University of Western Ontario <i>"Calpain in diabetes-associated myocardial hypertrophy and fibrosis"</i>
9:30AM – 9:45AM	Pimthanya Wanichawan, University of Oslo "Calpain induces cleavage of the cardiac Na+/Ca2+ exchanger 1 (NCX1) in pressure-overloaded hearts: Molecular interactions and identification of a calpain cleavage site"
9:45AM – 10:15AM	Yunchao Su, Medical College of Georgia, Augusta, GA <i>"Calpain in pulmonary vascular remodeling"</i>
10:15AM – 10:45AM	FASEB Sponsored Coffee Break
10:45AM – 11:15AM	Kinya Otsu, King's College "Conventional calpains protect the heart"
11:15AM – 11:30AM	Venkateswaran Subramanian, University of Kentucky "Calpain-2 compensation promotes angiotensin II-induced ascending and abdominal aortic aneurysms in Calpain-1 deficient mice"
11:30AM – 11:45AM	Ines Araújo, University of Coimbra, Portugal "Calpains and neurogenesis: Impairment of neural stem cell proliferation and neuroblast migration in calpastatin-/- mice"
11:45AM – 12:15PM	Business Meeting

12:15PM – 1:15PM Lunch

Free Afternoon

1:00PM – 6:00PM	Optional Organized Group Activity
6:00PM – 7:00PM	Dinner
Session 8: 7:00PM – 9:45PM	Calpains in Muscle Session Chair Elisabeth Huff-Lonergan, Iowa State University
7:00PM - 7:30PM	Elisabeth Huff-Lonergan, Iowa State University "Biochemistry of muscle: Relevance of postmortem changes to aging"
7:30PM – 8:00PM	Melissa Spencer, University of California, Los Angeles "Defective activation of cell signaling pathways underlies limb girdle muscular dystrophy type 2A (calpainopathy)."
8:00PM – 8:15PM	William Lostal, Généthon "Restriction of Calpain 3 expression to the skeletal muscle prevents cardiac toxicity and corrects pathology in a murine model of Limb- Gridle Muscular Dystropy"
8:15PM – 8:30PM	Break
8:30PM – 8:45PM	Robyn Murphy, La Trobe University "Calpastatin and m-calpain have different cellular localizations in rat skeletal muscle: implications for function"
8:45PM – 9:15PM	Carol Lorenzen, University of Missouri-Columbia "Calpastatin biosensors"
9:15PM – 9:30PM	Yasuko Ono, Tokyo Metropolitan Institute of Biomedical Science "PLEIAD/SIMC1/C5orf25, a novel autolysis regulator for a skeletal muscle-specific calpain, CAPN3, scaffolds a CAPN3 substrate, CTBP1"
9:30PM – 9:45PM	Kazuo Tonami, Tokyo Metropolitan Institute of Biomedical Science "Calpain 6 is a suppressor of skeletal muscle development and regeneration"

Friday,	
July 26,	2012
7:30AM - 8	3:30AM

AM

Session 9 8:30AM – 11:30PM

8:30AM – 8:40 AM Suzuki Award Winner--Predoctoral

Breakfast

8:45AM – 9:00AM Murachi Award Winner--Postdoctoral

9:30AM – 9:45AM Goll Award Winner—Junior Faculty

9:45AM - 10:00AM Break

10:00AM – 11:15AM Discussion and Planning for Next Conference

11:15AM – 11:30AM Closing Comments

11:30AM Departures Boxed Lunches Available

END OF CONFERENCE

Suzuki, Murachi, and Goll Awards

Jim Geddes and Peter Greer

For additional information contact: FASEB Summer Research Conferences 9650 Rockville Pike Bethesda, MD 20814

> vermont@faseb.org www.faseb.org/src

FASEB SCIENCE RESEARCH CONFERENCE POSTER SCHEDULE

No part of the conference proceedings, including this collection of abstracts, may be referenced. Please contact the authors directly for permission to cite their work.

Poster Session 1 – Monday PM

- #1. <u>Yuki Maemoto</u>, Satomi Kiso, Hideki Shibata and Masatoshi Maki Analyses of ESCRT-dependent limited proteolytic activities of calpain-7 in mammalian cells
- #2. <u>P. Wanichawan</u>, T.L. Hafver, I. G. Lunde, J. M. Aronsen, M. Lunde, H. Kvaløy, T. Tønnessen, I. Sjaastad, O. M. Sejersted and C. R. Carlson Calpain induces cleavage of the cardiac Na+/Ca2+ exchanger 1 (NCX1) in pressure-overloaded hearts: Molecular interactions and identification of a calpain cleavage site
- #3. <u>Hui Shi</u>, Ting Tao, Yihong Guan, Delai Huang, Ye Chen, David P Lane, Jun Chen, Jinrong Peng Def defines a conserved nucleolar pathway that leads p53 to proteasome-independent degradation
- #4. <u>Delai Huang</u>, Ting Tao, Hui Shi, Jinrong Peng Def Functions As A Cell Autonomous Factor in Organogenesis of Digestive Organs in Zebrafish
- #5. <u>Viktor Demko</u>, Kamran-Shalchian Tabrizi, Sen Zhao, Zhe Liang, Wenche Johansen, Robert Wilson, Odd-Arne Olsen *The evolutionary history of eukaryotic calpains displays multiple variants of regulatory mechanisms for CysPc activity*
- #6. <u>Jeannette Hübener</u>, Jonasz Jeremiasz Weber, Huu Phuc Nguyen, Olaf Riess Strategies for analyzing calpain-mediated ataxin-3 cleavage in the molecular pathogenesis of SCA3
- #7. <u>Kazuo Tonami</u>, Shoji Hata, Koichi Ojima, Yasuko Ono, Tomokazu Amano, Yukiko Kurihara, Kazunori Nakajima, Hiroki Kurihara, and Hiroyuki Sorimachi *Calpain-6 is a suppressor of skeletal muscle development and regeneration*
- #8. <u>Shoji Hata</u>, Fujiko Kitamura, and Hiroyuki Sorimachi G-calpain is a heterodimer of CAPN8 and CAPN9, which mainly play catalytic and regulatory roles, respectively
- #9. <u>Mala V. Rao</u>, Mary Kate McBride, Jabbar Campbell, Asok Kumar, Audrey Hashim, Henry Sershen, Philip H. Stavrides, Masuo Ohno, Karen E. Duff, Michael Hutton, and Ralph A. Nixon Calpastatin inhibits Cdk5 activation, tau hyperphosphorylation, tau oligomer formation to delay disease onset and increase survival times in JNPL3 mice

- #10. <u>Peter R. Hoffmann</u>, FuKun W. Hoffmann, Aaron H. Rose, Pietro Bertino, Jiro Takano, Nobuhisa Iwata, Takaomi C. Saido, Zhi Huang *Calpastatin prevents NF-κB mediated hyperactivation of macrophages and attenuates colitis*
- #11. <u>Yasuko Ono</u>, Shun-ichiro Iemura, Stefanie M. Novak, Naoko Doi, Fujiko Kitamura*, Tohru Natsume, Carol C. Gregorio, and Hiroyuki Sorimachi PLEIAD/SIMC1/C5orf25, a novel autolysis regulator for a skeletal muscle-specific calpain, CAPN3, scaffolds a CAPN3 substrate, CTBP1
- #12. F<u>umiko Shinkai-Ouchi</u>, Suguru Koyama, Shoji Hata, Mika Ueno, Mayumi Shindo, Yasuko Ono, Hiroshi Mamitsuka, Hiroyuki Sorimachi *Towards understanding the "substrate specificity" of calpain by proteomics and bioinformatics*
- #13. <u>Venkateswaran Subramanian</u>, Jessica J. Moorleghen, Anju Balakrishnan, Deborah A. Howatt, Athar H. Chishti, Haruhito Adam Uchida. *Calpain-2 Compensation Promotes Angiotensin II-induced Ascending and Abdominal Aortic Aneurysms in Calpain-1 Deficient Mice*
- #14. <u>R.M. Murphy</u>, J.P. Mollica and G.D. Lamb Calpastatin and m-calpain have different cellular localizations in rat skeletal muscle: implications for function
- #15. <u>Nechama S. Kosower</u> Mycoplasma and lipid-containing agonists for Toll-Like Receptor 2 (TLR2) upregulate calpastatin: possible treatment of calpain-related disorders
- #16. <u>Yubin Wang</u>, Xiaoning Bi, Michel Baudry Neuroprotection elicited by activation of synaptic NMDA receptors involves calpain-mediated degradation of PHLPP1 and Akt and ERK1/2 activation
- #17. <u>Guoqi Zhu</u>, Yubin Wang, Victor Briz, Yu-Tien Hsu, Xiaoning Bi and Michel Baudry Dual and opposite functions for calpain in long-term potentiation induction and consolidation
- #18. <u>Victor Briz</u>, Mariam Avetysiam and Michel Baudry Local synthesis of RhoA and LIMK contributes to BDNF-induced actin polymerization in hippocampal slices
- #19. <u>Kristin E. Low</u>, Serge Zaretsky, Kevin Chen, Spencer Ler, Robert L. Campbell, Andrei K. Yudin, and Peter L. Davies. *Calpain-specific cyclic peptide inhibitors: one good turn deserves another*

Poster Session 2 – Wednesday PM

- #20. <u>Elisa M. Floriddia</u>, Miriam Jakubik, Pierluigi Nicotera, and Daniele Bano Role of the calpain system in adult neuronal precursor and differentiated cells
- #21. Takuro Miyazaki, Yoshitaka Taketomi, Masafumi Takimoto, Makoto Murakami, Akira Miyazaki m-Calpain is induced in vascular endothelial cells on human and mouse atheromas and accelerates atherosclerotic lesion development through proteolytic disorganization of VE-cadherin
- #22. <u>Pablo Pánico</u>, Anna Lilia Burns, Monserrat Sordo, Melquisedec Esquivel, Patricia Ostrosky-Wegman, Ana María Salazar The effects of arsenic exposure on calpain-10 expression and calpain activity in human lymphocytes
- #23. <u>William Lostal</u>, Carinne Roudaut, Florence Le Roy, Laurence Suel, Jerome Poupiot, Karine Charton, Marc Bartoli, Isabelle Richard *RESTRICTION OF CALPAIN3 EXPRESSION TO THE SKELETAL MUSCLE PREVENTS CARDIAC TOXICITY AND CORRECTS PATHOLOGY IN A MURINE MODEL OF LIMB-GIRDLE MUSCULAR DYSTROPHY*
- #24. <u>Maike Breiden</u> & Michael Ehrmann Human calpain 2 and HTRA1 form a protease complex in vitro
- #25. <u>Koichi Ojima</u>, Yasuko Ono, Shoji Hata, Oe Mika, Ikuyo Nakajima, Susumu Muroya, Koichi Chikuni, Hiroyuki Sorimachi *Identification of phosphorylation sites of muscle-specific calpain-3*
- #26. <u>VM Machado</u>, BP Carreira, MM Azevedo1, MI Morte, J Takano, N Iwata, TC Saido, CM Carvalho, IM Araújo Calpains and neurogenesis: Impairment of neural stem cell proliferation and neuroblast migration in calpastatin-/- mice
- #27. <u>Vinit B. Mahajan</u>, Katherine J. Wert, M.S., M.Phil, Jessica M. Skeie, Stephen H. Tsang
 Calpain-5 Retinopathy in Mice Using a Human CAPN5-R243L Lentiviral Vector
- #28. <u>James MacLeod</u>, Jing Hu, David Otasek, Waheed Sangrar, Igor Jurisica, and Peter Greer The role of calpains-1 and -2 in promoting mammary tumorigenesis
- #29. <u>Chen Guang Yu</u> and James W. Geddes. Targeting calpain 1 and its cross-talk with ERK1/2 signaling pathway in pain hypersensitivity after spinal cord injury
- #30. <u>Rogers C.B.</u>, Ghoshal S., Nelson P.T., Geddes J.W. Alterations in calpain isoform expression and activation in mild cognitive impairment compared to Alzheimer's disease

- #31. <u>Marco I. González</u> and Philip Lam The Role of Calpain-Dependent Proteolysis in Epileptogenesis
- #32. <u>Simin Lu</u>, Fumihiko Urano *m-calpain induces neuronal and beta cell death in Wolfram Syndrome*
- #33. <u>Christian-Scott E. McCartney</u>, Stacy Visser-Grieve, Peter A. Greer, and Peter L. Davies Development of PLFAER into a fluorescent protein-based FRET substrate
- #34. <u>Stacy Visser-Grieve</u>, Jun Inoue and Peter Greer. Calpain mediates sensitivity to targeted therapeutics in breast cancer cells
- #35. <u>Ranjana Singh</u>, Charles Mashburn, Dingyuan Lou, Sarbani Ghoshal, Brantley Graham and James W. Geddes *Calpain 5 is highly expressed in the brain, abundant in the nucleus, and associated with promyelocytic leukemia protein bodies*
- #36. J.D.Morton, Y. Muto and D.N. Palmer Effect of muscle stretching on post-mortem calpain activity
- #37. <u>Christopher M. Norris</u>, Hafiz Abdul Mohmmad, Rodney P. Guttmann Calpain interactions with the protein phosphatase calcineurin in Alzheimer's disease
- #38. <u>Rui Ni</u>, Qiang Wang, Futian Tang, Tao Sun, Dong Zheng, Huaqing Zhu, Yong Yu, Ruizhen Chen, Peter W Schiller, Peter A Greer, Tianqing Peng Calpain-1 accumulation in mitochondria contributes to ROS generation which mediates TNF-α expression in endotoxemic heart