

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
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NAME Peter James Dempsey, Ph.D.		POSITION TITLE Principal Investigator	
eRA COMMONS USER NAME (credential, e.g., agency login) pjdempsey		Associate Professor, Pediatrics and Communicable Diseases and Associate Professor of Molecular and Integrative Physiology	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Post-doctoral Fellow, Vanderbilt University, Nashville, TN		1990-1994	Tumor Biology
Post-doctoral Fellow, MSKCC, New York, NY		1989-1990	Tumor Biology
University of Melbourne & Ludwig Institute for Cancer Research, Melbourne, Australia	Ph.D.	1988	Tumor Biology
University of Melbourne, Melbourne, Australia	B.S. (Honors)	1980	Biochemistry & Pharmacology
University of Melbourne, Melbourne, Australia	B.S.	1979	Biochemistry & Pharmacology

**A. Positions and Honors**

- 1977-1978 Victorian Education Scholarship  
 1980 Bachelor of Science (Honors) (First Class H1)  
 1981-1984 Australian Post-Graduate Research Scholarship  
 1993-1994 National Service Research Award, U.S. National Academy of Sciences  
 1995-2000 Research Assistant Professor, Depts. of Medicine and Cell Biology, Vanderbilt University Medical School, Nashville, TN.  
 2000 Senior scientist, Molecumetics, Bellevue, WA  
 2000-2006 Principal Investigator, Pacific Northwest Research Institute, Seattle WA  
 2003-2006 Assistant Professor, Div of Metabolism, Endocrinology and Nutrition, Dept. of Medicine, University of Washington  
 2006-Present Associate Professor, Dept. of Pediatrics and Molecular and Integrated Physiology, University of Michigan  
 2008-Present Brehm Investigator, University of Michigan  
 2008-Present Director of Research, Core Facility, Dept. of Pediatrics, University of Michigan

**B. Selected peer-reviewed publications (from over 60 publications)**

1. Eguchi S, **DEMPSEY PJ**, Frank G, Motley ED and Inagami T. Distinct effects of metalloprotease inhibitor on the activation of MAP kinases by AngiotensinII. Possible requirement of metalloprotease-dependent EGF receptor transactivation for the p38 PAP kinase activation. JBC, 276:7957-62, 2001. PMID: 11116149
2. Brown CL, Coffey RJ and **DEMPSEY PJ**. The Cytoplasmic Domain of Human Amphiregulin Precursor Confers Basolateral Sorting but is Not Essential for Metalloprotease Inhibitor-Sensitive Processing of its Ectodomain. JBC, 76:29538-49, 2001. PMID: 11382759
3. Garton KJ, Gough PJ, Blobel CP, Murphy G, Greaves DR, **DEMPSEY PJ**, Raines EW. TACE (ADAM17) mediates the cleavage and shedding of Fractalkine (CX3CL1). J Biol Chem. 2001 Oct 12;276(41):37993-8001. Epub 2001 Aug 8. PMID: 11495925
4. **DEMPSEY PJ**, Garton KJ and Raines EW. Emerging roles of TACE as a key protease in ErbB ligand shedding. Molecular Interventions 2:136-141, 2002. PMID: 14993373
5. Saito S, Frank GD, Motley ED, **DEMPSEY PJ**, Utsunomiya H, Inagami T, Eguchi S. Metalloprotease inhibitor blocks angiotensin II-induced migration through inhibition of epidermal growth factor receptor transactivation. Biochem Biophys Res Commun. 2002 Jun 28;294(5):1023-9. PMID: 12074579 .

6. **DEMPSEY PJ**, Meise KS and Coffey,RJ. Basolateral Sorting of Pro-Transforming Growth Factor-alpha in Polarized Epithelial Cells: Characterization of Cytoplasmic Domain Determinants. *Exp Cell Res.* 2003 May 1;285(2):159-74. PMID: 12706112
7. Frank GD, Inagami T, Saito S, Ohba M, Sasaki T, Higashiyama S, **DEMPSEY PJ** and Eguchi S. Distinct Mechanisms of receptor and non-receptor tyrosine kinase activation by H<sub>2</sub>O<sub>2</sub> in vascular smooth muscle cells; Role of metalloprotease and PKC- $\delta$  . *Mol Cell Biol.* 2003 Mar;23(5):1581-9. PMID: 12588978
8. Garton KJ, Gough PJ, Philalay J, Blobel C, **DEMPSEY PJ**, Raines EW. Stimulated shedding of vascular cell adhesion molecule 1 (VCAM-1) is mediated by tumor necrosis factor- $\alpha$  – converting enzyme (ADAM17). *J Biol Chem.* 2003 Sep 26;278(39):37459-64. Epub 2003 Jul 23. PMID: 12878595 .
9. Gough PJ, Garton, KJ, Wille PT, Rychlewski M, **DEMPSEY PJ** and Raines EW. ,ADAM10-mediated cleavage and shedding regulates the cell surface expression of CXCL16/SR-PSOX. *J Immunol.* 2004 Mar 15;172(6):3678-85. PMID: 15004171
10. Mifune M, Frank GD, Inagami T, Motley ED, Utsunomia H, **DEMPSEY PJ** and Eguchi S., Signal transduction of Betacellulin in growth and migration of vascular smooth muscle cells. *Am J Physiol Cell Physiol.* 2004 Sep;287(3):C807-13. Epub 2004 May 26. PMID: 15163624
11. Sanderson MP, Erickson SN, Gough PJ, Garton KJ, Wille PT, Raines EW, Andrew J, Dunbar AJ and **DEMPSEY PJ**. ADAM10 mediates ectodomain shedding of the betacellulin precursor activated by p-aminophenylmercuric acetate and extracellular calcium influx. *J Biol Chem.* 2005 Jan 21;280(3):1826-37. Epub 2004 Oct 26. PMID: 15507448
12. Franklin JL, Yoshiura K, **DEMPSEY PJ**, Bogatcheva G, Jeyakumar L, Meise KS, Pearsall RS, Threadgill DW and Coffey RJ. Identification of MAGI-3 as a Transforming Growth Factor-alpha Binding Protein. *Exp Cell Res.* 2005 Feb 15;303(2):457-70. PMID: 15652357
13. Mifune M, Ohtsu H, Frank GD, Suzuki H, Nakashima H, Brailoiu E, Dun NJ, Tadashi Inagami T, Higashiyama S, Thomas WG, Sadoshima J, Eckhart AD, **DEMPSEY PJ**, and Eguchi S. G Protein Coupling and Second Messenger Generation are indispensable for ADAM17-dependent Heparin-Binding EGF Shedding through Angiotensin II Type 1 Receptor. *J Biol Chem.* 2005 Jul 15;280(28):26592-9. Epub 2005 May 19. PMID: 15905175
14. Ohtsu H, **DEMPSEY PJ** and Eguchi S. ADAMs as mediators of EGF receptor transactivation by G protein-coupled receptors. *Am J Physiol Cell Physiol.* 2006 Jul;291(1):C1-10. Review. PMID: 16769815
15. Sanderson MP, **DEMPSEY PJ** and Dunbar AJ. Control of ErbB signaling through metalloprotease mediated ectodomain shedding of EGF-like factors. *Growth Factors*, 24:121-136, 2006. *Growth Factors.* 2006 Jun;24(2):121-36. Review. PMID: 16801132
16. Sanderson MP, Abbott CA, Tada H, Seno M, **DEMPSEY PJ**, and Dunbar AJ. Two independent mechanisms involving reactive oxygen species and calcium signaling regulate ectodomain shedding of the betacellulin precursor. *J Cell Biochem.* 2006 Oct 1;99(2):609-23. PMID: 16676357
17. Ohtsu H, **DEMPSEY PJ**, Frank GD, Higuchi S, Suzuki H, Nakashima H, Eguchi K and Eguchi S. ADAM17 mediates EGF receptor by angiotensin II in vascular smooth muscle cells. *Arterioscler Thromb Vasc Biol* 26:133-7, 2006. *Arterioscler Thromb Vasc Biol.* 2006 Sep;26(9):e133-7. Epub 2006 Jul 13. PMID: 16840716
18. Li N, Wang Y, Forbes K, Vignali KM, Heale BS, Saftig P, Hartmann D, Black RA, Rossi JJ, Blobel CP, **DEMPSEY PJ**, Workman CJ, and Vignali DA. Metalloproteases regulate T-cell proliferation and effector function via LAG-3. *EMBO J.* 26:494-504, 2007. *EMBO J.* 2007 Jan 24;26(2):494-504. PMID: 17245433
19. Li N, Boyd K, **DEMPSEY PJ** and Vignali DAA. Non-cell autonomous expression of TNF $\alpha$  converting enzyme (TACE/ADAM17) is required for normal lymphocyte development. *J. of Immunology.* 178: 4214-21, 2007. *J Immunol.* 2007 Apr 1;178(7):4214-21. PMID: 17371977
20. Moss ML, Bomar M, Liu Q, Sage H, **DEMPSEY PJ**, Lenhart PM, Gillispie PA, Stoeck A, Wildeboer D, Bartsch JW, Palmisano R, and Zhou P. The ADAM10 prodomain is a specific inhibitor of ADAM10 proteolytic activity and inhibits cellular shedding events. *J. Biol. Chem.* 282(49):35712-21. Epub 2007. PMID: 17895248
21. Sanderson MP, Keller S, Alonso A, Riedle S, **DEMPSEY PJ**, and Altevogt P. Generation of novel secreted epidermal growth factor receptor (EGFR/ErbB1) isoforms via metalloprotease-dependent ectodomain shedding and exosome secretion. *J Cell Biochem.* 2008 Apr 15;103(6):1783-97. PMID: 17910038
22. Moss ML, Stoeck A, Yan W and **DEMPSEY PJ**. ADAM10 as a target for anti-cancer therapy. *Current Pharm. Biotech.* 9(1):2-8, 2008. *Curr Pharm Biotechnol.* 2008 Feb;9(1):2-8. Review. PMID: 18289051
23. Merchant NB, Rogers, CM, Rothenberg M, Graves-Deal R, **DEMPSEY PJ** and Coffey RJ. Blockade of the Epidermal Growth Factor Receptor Axis results in Cooperative Growth Inhibition of Colon cancer Cells. *15;14(4):1182-91* 2008. *Clin Cancer Res.* 2008 Feb 15;14(4):1182-91. PMID: 18281553

24. Nakashima H, Frank GD, Shirai H, Hinoki A, Higuchi S, Ohtsu H, Eguchi K, Sanjay A, Reyland ME, **DEMPSEY PJ**, Inagami T, and Eguchi S. Novel Role of Protein Kinase C Delta Tyr311 Phosphorylation in Vascular Smooth Muscle Cell Hypertrophy by Angiotensin II. *Hypertension*. 51(2):232-8. 2008 *Hypertension*. 2008 Feb;51(2):232-8. Epub 2008 Jan 7. PMID: 18180404
25. Gelling RW, Yan W, Al-Noori S, Pardini A, Morton GJ, Ogimoto K, Schwartz MW, **DEMPSEY PJ**. Deficiency of TNF $\alpha$  Converting Enzyme (TACE/ADAM17) Causes a Lean, Hypermetabolic Phenotype in Mice. *Endocrinology*. 2008 Dec;149(12):6053-64. Epub 2008 Aug 7. PMID: 18687778
26. Yan F, Hanwei C, Chaturvedi R, Krishna U, Hobbs SS; **DEMPSEY PJ**; Peek Jr MR, Cover TL, Washington MK, Wilson KT, and Polk DB. Epidermal growth factor receptor activation protects gastric epithelial cells from *Helicobacter pylori*-induced apoptosis. *Gastroenterology* 2009 Apr;136(4):1297-1307, e1-3. Epub 2009 Jan 1. PMID: 19250983
27. Crawford HC, **DEMPSEY PJ**, Brown G, Adam L, Moss ML. ADAM10 as a therapeutic target for cancer and inflammation. *Curr Pharm Des*. 2009;15(20):2288-99. PMID: 19601831
28. Moss M, Powell G, Edwards I, Williams J, Petrovich R, Liu, Q, Zhou P, Blumenkron F, Lipsky P, Stoeck A, **DEMPSEY PJ**, Ferdous T, and Bartsch JW. Inhibition of Adam9 by its prodomain reveals Adam10 independent shedding for the low affinity IgE receptor cd23 in human B-cells (submitted to JBC).
29. Stoeck A, Yan W, Shang L and **DEMPSEY PJ**. Sequential and g-secretase-dependent BTC processing generates an intracellular domain fragment that inhibits cell growth (submitted to J Cell Science).
30. Shang L, Yan W, Stoeck A and **DEMPSEY PJ**. BTC shedding protects against oxidative stress-induced b-cell apoptosis (submitted to JBC).
31. Stoeck A, VanDussen K, Shang L, Yan W, Samuelson LC, Crawford HC and **DEMPSEY PJ**. Adam10 (Kuzbanian) Is Required For Cell Lineage Specification Of Intestinal Crypt Stem Cells (in preparation for Nature Genetics).
32. Yan W, Gillispie PA, and **DEMPSEY PJ**. HB-EGF Deficient Mice Display Glucose Intolerance And Beta Cell Dysfunction (in preparation for Diabetes).

### C. Research Support

#### Ongoing Research Support

200603MOP-610 676-E-ADWY4157 7 Prentki (PI) 10/01/06-0/30/09

Candian Institute of Health Research (CIHR)

Regulation of GLP-1 induced EGFR transactivation in beta cells

The goals of this project are to determine the role of GLP-1 induced ErbB transactivation in Beta Cell proliferation.

Role: Co-Investigator

1-2008-473 Dempsey (PI) 09/01/2008–08/31/2011

Juvenile Diabetes Research Foundation (JDRF)

Betacellulin and ErbB4 Receptor Signaling Axis In Adult Beta Cell Survival

The primary objective of this proposal is to elucidate the respective roles played by the dual specificity ligand betacellulin (BTC) and downstream ErbB4 receptor signaling on adult beta-cell regeneration through genetic studies using BTC gain-of-function and ErbB4 receptor loss-of-function mouse models.

Role: Principle Investigator

7R01 DK063363-05 Dempsey (PI) 09/30/2002–06/30/2008

NIH (no cost extension)

Endogenous Betacellulin Signaling in Beta-Cell Biology

The specific goals of this grant proposal are to investigate the roles of endogenous BTC signaling in cell proliferation, differentiation, neogenesis and survival.

Role: Principle Investigator

Training Grant Dempsey (PI) 01/01/2009-12/31/2009

Michigan Diabetes Research & Training Center

Role of ErbB4 receptor Signaling in the Central Regulation of Energy Metabolism

The primary objectives are to further characterize the role of ErbB4 receptor signaling axis on the central regulation of energy homeostasis.

Role: Principle Investigator

**Completed Research Support**

1R01 DK59778-01 Dempsey (PI)

09/01/2000 - 06/30/2007

NIDDK-NIH

Processing of EGF Ligands: Role in Gut Biology and Cancer

The major goals of this project are to determine the involvement of TNFalpha converting enzyme (TACE/ADAM17) and similar ADAMs in the ectodomain processing of EGF-like growth factor precursors, to characterize the mechanisms that regulate TACE activity and to examine the role of TACE in intestinal epithelial cells

Role: PI

CCFA Dempsey (PI)

07/01/2007 - 06/30/2008

Crohn's and Colitis Foundation Senior Research Award

ADAM-mediated ErbB signaling in mucosal injury and repair

The specific goals of this grant proposal are to investigate the regulation of ADAM17 activity in intestinal epithelial cells and to determine its role in ErbB transactivation and in mucosal injury and repair.

Juvenile Diabetes Research Foundation

Role: PI

JDRF Dempsey (PI)

09/01/2007 - 08/30/2008

5-2007-969

Novel Intracellular Signaling by the Betacellulin Cytoplasmic Tail Fragment

The primary objectives are to biochemically characterize the betacellulin intracellular domain fragment (BTC-ICD) and to determine whether it has unique intracellular signaling properties that are beneficial for beta cells.