

Curriculum Vitae

MAQSOOD A. CHOTANI, PhD

Principal Investigator
Center for Cardiovascular & Pulmonary Research
Research Institute at Nationwide Children's Hospital
Assistant Professor, Department of Pediatrics
The Ohio State University
Wexner 307, 700 Children's Drive
Columbus, Ohio 43205 USA
Telephone: (614) 355-4516
maqsood.chotani@nationwidechildrens.org

Citizenship

United States

Education

1990-1997

Ph.D., August, 1997
The Ohio State University, Columbus, Ohio
Interdisciplinary Graduate Program in Molecular, Cellular &
Developmental Biology
Dissertation Advisor: Ing-Ming Chiu, Ph.D.

Dissertation Committee: Lee F. Johnson, PhD
Deborah S. Parris, PhD
Long-Sheng Chang, PhD

1985-1988

B.A., September, 1988
The College of Wooster, Wooster, Ohio
Major: Biology Minor: Chemistry
Advisors: Donald Wise, Ph.D.
Clague P. Hodgson, Ph.D.

Professional Experience

Feb 2009 - Present

Assistant Professor
Department of Pediatrics
Ohio State University Medical Center

June 2009-Present

Graduate faculty member, *Biomedical Sciences Graduate Program* (BSGP), and the Interdisciplinary *Molecular, Cellular, & Developmental Biology* (MCDB) Graduate Program, Ohio State University

August 2008 - Present

Principal Investigator
Center for Cardiovascular & Pulmonary Research, Research
Institute at Nationwide Children's Hospital

January 2004-Present

Member, Ohio State University Davis Heart & Lung Research
Institute

- March 2002 - July 2008
Research Scientist
Ohio State University Davis Heart & Lung Research
Institute
- March 1998 - Feb 2002
Postdoctoral Researcher/Fellow
Ohio State University Davis Heart & Lung Research
Institute (*field of study: Vascular Biology/Molecular Physiology*)
- Oct. 1997 - Feb. 1998
Postdoctoral Researcher
Ohio State University, Department of Internal
Medicine (*field of study: Molecular & Cell Biology*)
- Sept.1990 - Sept. 1997
Graduate Research Associate, 1992-Sept.1997
Ohio State University
– Cell and molecular biology approaches to study
growth factor gene regulation
Graduate Teaching Associate, 1990-1992
– Teaching Assistant in General Biology
- 1988-1990
Jr. Research Associate
MetroHealth Medical Center, Cleveland, Ohio
Department of Psychiatry
– Purification of platelet plasma membrane for
studies related to clinical depressive illness and
Alzheimer's disease
– Radioligand binding analyses of cell receptors
– Anisotropy studies
– Metabolite analysis using gas chromatography
Employer: John E. Piletz, Ph.D.
- 1988 (June-Sept.)
Ohio Agriculture Research & Development Center,
Department of Preventive Veterinary Medicine, Food Animal
Health Research Program, Wooster, Ohio
Laboratory Technician
– Processing of field samples for studies on
transmissible gastroenteritis virus
– Infection of cells *in vitro*
– Detection, purification and propagation of virus
– Providing virus pools to co-workers for molecular
hybridization studies
Employer: Linda J. Saif, Ph.D.
- 1985-1988
Department Assistant, Biology Dept., College of Wooster
(academic year 1987-1988)
Department Assistant, Physics Department, College of Wooster
(academic year 1986-1987)
Supervisor, Food Service, College of Wooster (Sept-Dec 1986)
Crew person, Food Service, College of Wooster, Jan1985-May

1988)

Honors

Local

Sigma Xi and Phi Beta Kappa, 1988

Honors, Senior Independent Study Thesis, 1988, The College of Wooster, Wooster, Ohio

Department honors (Biology), 1988, The College of Wooster, Wooster, Ohio

Horace N. Mateer Prize in Biology, 1988, The College of Wooster, Wooster, Ohio

Awardee, May 10, 1994, The 20th annual ICSABER Society Graduate Student Forum, The Ohio State University, Columbus, Ohio

Awardee, April 4, 2002, The First Annual Integrated OSU Medical Center Graduate & Postgraduate Research Day, The Ohio State University, Columbus, Ohio

National

Awardee, Young Scientist Travel Award for the joint American Society for Biochemistry & Molecular Biology/American Society for Pharmacology & Experimental Therapeutics meeting in Boston (June 4-June 8, 2000)

Awardee, Young Scientist Travel Award for the 10th International Symposium on Vascular Neuroeffector Mechanisms, Granlibakken, Lake Tahoe, California (July 12-15, 2002)

International

Gold Medal & cash award, Pakistan Academy of Sciences, recognizing scientific contributions of Pakistani scientists in the field of Medical Sciences (2004)

Activities

Extracurricular

Volunteer Medic-Aide, Wooster Community Hospital (June-August 1986)

Hotline volunteer, February 1989- February 1990, The Cleveland Rape Crisis Center, Cleveland, Ohio

Sustaining supporter (1995-Present), The Wooster Fund, The College of Wooster

Maqsood A. Chotani, PhD

Sustaining supporter (2009-present), Nationwide Children's Hospital (NCH) teams, Pelotonia and AHA Heart Walk, American Cancer Society, NCH Foundation, Mid-Ohio Foodbank

Academic

Phi Beta Kappa (sustaining supporter, liberal arts education, up to 2003)

Secretary/treasurer, 1992-1995, Molecular, Cellular, and Developmental Biology Graduate Student Organization
The Ohio State University, Columbus, Ohio

Organizer and Executive Committee member, *Davis Heart & Lung Research Institute Postdoctoral Scholars Association* (2002-2004).

Organizing Committee, *College of Medicine & Public Health Office of Postdoctoral Programs*, The Ohio State University (October 2003-January 2004). Office opened Sept 2005.

Member, Education Committee, Davis Heart & Lung Research Institute (September 2002-June 2005)

Member, Cores Operations Committee, Davis Heart & Lung Research Institute (October 2005-July 2007)

Davis Heart & Lung Research Institute Study Section, Intramural Thematic Grants Program, (Spring 2007 cycle), The Ohio State University, Columbus, Ohio

Steering Committee, *First Annual, Second Annual, and Third Annual Integrated Health Science Graduate and Postgraduate Research Day*, The Ohio State University College of Medicine (April 4, 2002, April 3, 2003, and April 1, 2004)

Judge, *Sixth Annual OSUMC Graduate and Postgraduate Research Day*, The Ohio State University College of Medicine (March 29, 2007), Columbus, Ohio

Judge, *Eighth Annual OSUMC Research Day* (April 2, 2009), Columbus, Ohio

Judge, *Ninth Annual OSUMC Research Day* (April 8, 2010), and 2010 Annual Research Conference, The Research Institute at Nationwide Children's Hospital (April 6-7, 2010), Columbus, Ohio

Judge, 2011 Research Celebration—combined OSU and NCH (10th Annual OSUMC Trainee Research Day (April 7, 2011), and The Research Institute at Nationwide Children's Hospital Annual Poster Day Competition (April 6, 2011).

Judge, *Second Annual Research Day 2007*, Division of

Pulmonary, Allergy, Critical Care & Sleep Medicine, The Ohio State University Medical Center (September 28, 2007)

Judge, *Third Annual Research Day 2008*, Division of Pulmonary, Allergy, Critical Care & Sleep Medicine, The Ohio State University Medical Center (September 19, 2008)

Judge, *Third Annual Dorothy M. Davis Heart & Lung Research Institute Research Retreat Abstract Competition*, The Ohio State University Medical Center (October 21, 2008)

Judge, *10th Anniversary Research Day Dorothy M. Davis Heart & Lung Research Institute Research Retreat Abstract Competition*, The Ohio State University Medical Center (October 12, 2010, "A decade of discovery")

Judge, *The 14th, 15th, and 16th Annual Denman Undergraduate Research Forum* (May 13, 2009, May 12, 2010, and May 11, 2011), The Ohio State University Honors & Scholars Center, Undergraduate Research Office, and Office of Research (category Health Professions-Laboratory/Cellular, Speech & Hearing Science, Biological Sciences)

Center Representative,
Research Information Technology Advisory Committee (RITAC),
Research Institute at Nationwide Children's Hospital (June 2011-present)

Teaching

Autumn Quarter 2009: Molecular, Cellular & Developmental Biology (MCDB) 800/890 (two classes per week), The Ohio State University.

Summer 2009: Undergraduate Studies, Ryan C. Rauck, Pre-Medicine, Johns Hopkins University, Baltimore, Maryland; (Research, Biology 020.597, 3 course credits through Johns Hopkins).

Fall 2010: Undergraduate Studies, Robert Fidelibus, Chemical Engineering, Ohio State University, Columbus, Ohio; PDATRICS #699, Class # 28436, 3 credits.

Summer 2010: Molecular, Cellular & Developmental Biology (MCDB) 693, Laboratory Rotations (June-August 2010), The Ohio State University.

Winter 2012: Molecular, Cellular & Developmental Biology (MCDB) 693, Laboratory Rotations (January-March 2012), The Ohio State University.

Spring 2012: Molecular, Cellular & Developmental Biology (MCDB) 693, Laboratory Rotations (March-June 2012), The Ohio State University.

Graduate Committee

Elizabeth C. McNally (Graduate Program in Education: Teaching & Learning), Graduate Faculty Representative final oral examination for doctoral degree entitled "*Examining literacy development: Differential participation in narratives and literacy practices in one linguistically diverse kindergarten classroom*" (August 6, 2010).

Brian E. Jan (Molecular, Cellular, and Developmental Biology), Graduate Committee member for non-thesis written and oral Master's examination entitled: "*Collagen and the Heart*" (December 12, 2011).

Nicholas T. Unger (Biophysics Graduate Program)
Master's Thesis Committee (Winter 2012)
Thesis Title: "*Blockade Of The Transient Receptor Potential Vanilloid (TRP) by Ruthenium Red Does Not Suppress Hypothalamic Neuronal Thermosensitivity*".

Zoltan I. Buzas (Political Science), Graduate Faculty Representative Final Oral examination for doctoral degree entitled "*Race and International Politics: How Racial Prejudice Can Shape Discord and Cooperation among Great Powers*" (June 29, 2012).

Undergraduate Committee

Robert Fidelibus, Chemical Engineering, Undergraduate Honors Research Thesis Committee, Ohio State University, Columbus, Ohio (Spring 2012)
Thesis Title: "*Peptide expression and purification to elucidate the mechanism of vascular α_{2C} -adrenoceptor translocation*".

Editorial Assistance

- Contributor, "Paper Alerts: Pharmacology", *Current Opinion in Pharmacology* (January 2001- September 2002)
- Assistant to the Guest Referee Editor, *American Journal of Physiology* (Fall 2001)
- Ad Hoc reviewer
 - J. Pharmacology & Experimental Therapeutics*
 - Life Sciences*
 - Clinical Autonomic Research*
 - Journal of Cellular & Molecular Medicine*

Mentoring:**Past and Current Trainees**

1. Paul N. El-Dahdah, BS (post-graduate). Current position: medical student, Ohio University, Athens, Ohio. Paul was a Research Assistant in my lab.
2. Ryan C. Rauck (undergraduate). Current position: medical student, Ohio State University, College of Medicine.
Ryan was a Pre-Medicine student at Johns Hopkins University, Baltimore, Maryland. Ryan worked in my lab during the summer of 2009 and received 3 course credits through Johns Hopkins University for Research (Biology 020.597). His primary project involved structure-function studies on the G protein coupled α_2 -adrenoceptors (α_{2A} - and α_{2C} -adrenoceptors). Specifically, domain swapping studies to elucidate the role of the carboxyl terminus in regulating receptor trafficking. He presented this work at the annual undergraduate Tri-Beta Biology Honor Society poster session at Johns Hopkins, and graduated with honors.
3. Robert Fidelibus (undergraduate, Aug 24, 2010 – June 7, 2012). Undergraduate studies, Chemical Engineering, Ohio State University, Columbus, OH.
Robert was selected as an American Physiological Society (APS) Undergraduate Summer Research Fellow for 2011. Robert was one of 24 national winners. Robert's project was developed further for an honors thesis for his graduation. He presented his work at the national Experimental Biology 2012 meeting in San Diego, CA. Robert recently accepted a position with The Dow Chemical Company (Engineers Driven for Growth & Excellence (Edge) Program) in New Orleans, LA.
4. Joel Eversole, BS (post-graduate, March 15, 2011 – July 31, 2012). Volunteer trainee. Joel is submitting applications to schools with a graduate program in Physician Assistant Studies (PA Program).
5. Nicholas T. Unger, BA, MS. Current position: Research Associate, Center for Cardiovascular & Pulmonary Research, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio. Nick was initially a Research Assistant in my lab. He recently completed his Master's degree and transitioned to a full-time job with a local company.
6. Selvi C. Jeyaraj, PhD (Postdoctoral, March 2009 - March 23, 2012). Selvi was a trainee in my lab
at the Center for Cardiovascular & Pulmonary Research, The Research Institute at Nationwide Children's Hospital, Columbus, OH. Selvi was supported by a T32 training grant. She chose a career in teaching and was Adjunct Faculty, Department of Biological Sciences, Capital University, Columbus, OH, prior to her relocation to Kentucky.
7. Hanaa K.B. Motawea, MS (February 29, 2012 - Present). Hanaa is a visiting graduate student from Helwan University, Cairo, Egypt. She is currently a trainee in my laboratory.
8. Muzzammil Ahmed (March 16, 2012 – August 21, 2012). Muzzammil was a sophomore at Dublin Coffman High School, Dublin, OH, and was an Intern in my laboratory.

Rotation graduate students

9. Brian Jan (Molecular, Cellular and Developmental Biology Graduate Program, Ohio State University, June 28-July30, 2010).
10. Shengwei Chang (Molecular, Cellular and Developmental Biology Graduate Program, Ohio State University, July1-August 5, 2010).
11. James Boslett (Molecular, Cellular and Developmental Biology Graduate Program, Ohio State University, January 3, 2012- March 9, 2012)

12. Alisa Blazek (Molecular, Cellular and Developmental Biology Graduate Program, Ohio State University, March 26, 2012- June 7, 2012).

Research Support

Pending

1R01 HL119424-01
 “Molecular and Cellular Mechanisms of Vascular α_{2C} -adrenoceptor Translocation”
 NIH/NHLBI (October 2012 cycle)
Role on project: Principal Investigator (50%)

Graduate Research

Hanaa KB Motawea, Egyptian Government Scholarship
 Yearly allowance: \$30,297.50
 Annual research fees: \$10,000
 Plus comprehensive medical insurance, travel expenses

Completed Research Support

Institutional Training grant

“Training in Congenital and Acquired Heart Disease”
 Sponsor lab, T32 HL-098039 awarded to Selvi C. Jeyaraj (Postdoctoral Trainee), 1-1-2010 to 12-31-2011.
 Total amount: \$97,790: \$48,895/yr (\$42,204 stipend, \$2616 health insurance, \$2675 tuition, \$1400 travel)

Travel award

American Society for Biochemistry and Molecular Biology (ASBMB) travel award to Selvi C. Jeyaraj to present her work at the Experimental Biology 2010 meeting, Anaheim, CA (total amount \$1200).

Undergraduate Research

“Peptide expression and purification to elucidate mechanism of vascular α_{2C} -adrenoceptor mobilization”
 Host lab, American Physiological Society (APS) Summer Undergraduate Research Fellowship awarded to Robert Fidelibus for 10 weeks of summer research.
 Total amount \$5600: \$4000 stipend, \$1300 travel funds to present work at the Experimental Biology 2012 meeting in San Diego, \$300 to host lab, plus two years of complimentary undergraduate membership to APS.

Other Support

1. 1R21HL088087-01A1 (Exploratory/Developmental Research grant-R21) NIH/NHLBI
 Priority score: 146 Percentile: 11.9 (second submission, new investigator)
 “Mechanism of vascular α_{2C} -adrenoceptor mobilization”
 Direct costs: \$275,000 Indirect costs: \$137,500
 Start date: 03-04-2008 End date: 02-28-2012 (no-cost extension)
Summary: The major objective of this project is to study a novel interaction uncovered in a yeast genetic screen between α_{2C} -

Maqsood A. Chotani, PhD

adrenoceptors and the actin-binding protein filamin-2, and elucidate role in receptor mobilization by cyclic AMP signaling in vascular smooth muscle cells. Structure-function studies are proposed that will lead to the identification of filamin-2 binding domain in α_{2C} -adrenoceptors. These studies may be used to design synthetic decoy peptides to block this interaction and receptor mobilization, particularly as therapeutic intervention in peripheral vascular disease.

Role on project: Principal Investigator (30%)

2. Beginning Grant-in-Aid (0765204B)

American Heart Association, Great Rivers Affiliate

Priority score: 1.4571

Percentile: 14.2

"Targeting expression and mobilization of vascular α_{2C} -adrenoceptors"

Direct costs: \$110,000

Indirect costs: \$11,000

Start date: 07-01-2007

End date: 06-30-2010

Summary: The major goal of this study was to identify new targets for therapy aimed at early intervention for Raynaud's phenomenon. These studies utilized a novel in vitro model of human cutaneous arteriolar smooth muscle cells to elucidate the role of intracellular cyclic AMP-activated small G proteins Rap1 and Rho in α_{2C} -adrenoceptor expression and mobilization.

Role on project: Principal Investigator (25%)

3. Postdoctoral Fellowship 9920625V

American Heart Association, Ohio Valley Affiliate 14.91 percentile

7-1-99 to 6-30-01 (\$60,000)

"Role of α_2 -adrenoceptors in vascular smooth muscle cell biology: toward development of an in-vitro model for scleroderma"

Summary: The goal of this study was to identify and develop a cell-culture based system for examining expression and regulation of endogenous human α_2 -adrenoceptor subtypes in vascular smooth muscle cells.

Role on project: Principal Investigator (100%)

U.S. Patents

1. (No. 6,444,681; co-discoverer) *"Methods and compositions for treating Raynaud's Phenomenon and Scleroderma"*
2. *"Rap1A as a marker for cardiac arrhythmia"* (Chotani et al., filed 5-27-2012 (No. 31381/04028))

Other Memberships in Professional Organizations

American Association for the Advancement of Science
(1-30-98 to 1-21-02)

American Heart Association (Premium Professional Member - Silver Heart;
Council on Cardiovascular Disease in the Young and Council on Basic

Maqsood A. Chotani, PhD

Cardiovascular Sciences; 1998)

American Society for Pharmacology and Experimental Therapeutics (elected 2000, regular member)

American Society for Biochemistry and Molecular Biology (elected 2001, regular member)

American Physiological Society (elected 2010, regular member)

Peer-Reviewed Original Articles

- 1) Hodgson CP, Fisk RZ, Arora P, **Chotani M**. Nucleotide sequence of mouse virus-like (VL-30) retrotransposon BVL-1. *Nucleic Acids Res.* 18(3): 673; 1990 (PMID 2155410).
- 2) Piletz JE, Sarasua M, **Chotani M**, Saran A, Halaris A. Relationship between membrane fluidity and adrenoceptor binding in depression. *Psychiatry Res.* 38: 1-12; 1991 (PMID 1682966).
- 3) Piletz JE, Sarasua M, Whitehouse P, **Chotani M**. Intracellular membranes are more fluid in platelets of Alzheimer's disease patients. *Neurobiol of Aging.* 12: 401-406; 1991 (PMID 1770973).
- 4) Myers RL, Payson RA, **Chotani MA**, Deaven LL, Chiu I-M. Gene structure and differential expression of acidic fibroblast growth factor mRNA: identification and distribution of four different transcripts. *Oncogene.* 8: 341-349; 1993 (PMID 7678925).
- 5) Payson RA, Canatan H, **Chotani MA**, Wang W-P, Harris SE, Myers RL, Chiu I-M. Cloning of two novel forms of human acidic fibroblast growth factor (aFGF) mRNA. *Nucleic Acids Res.* 21(3): 489-495; 1993 (PMID 7680120).
- 6) Myers RL, Ray SK, Eldridge R, **Chotani MA**, Chiu I-M. Functional characterization of the brain-specific FGF-1 promoter, FGF-1.B. *J Biol Chem.* 270 (14): 8257-8266; 1995 (PMID 7713933).
- 7) **Chotani MA**, Payson RA, Winkles JA, Chiu I-M. Human fibroblast growth factor 1 gene expression in vascular smooth muscle cells is modulated via an alternate promoter in response to serum and phorbol ester. *Nucleic Acids Res.* 23(3): 434-441; 1995 (PMID 7533902).
- 8) **Chotani MA**, Chiu I-M. A recombinant PCR approach requiring only three non-chimeric primers to generate a minigene of interest. *Genetic Analysis: Biomol Eng.* 12(3-4): 133-135; 1996 (PMID 8673737).
- 9) **Chotani MA**, Chiu I-M. Differential regulation of human fibroblast growth factor 1 transcripts provides a distinct mechanism of cell-specific growth factor expression. *Cell Growth Differ.* 8(9): 999-1013; 1997. Erratum in 8 (11): 1241; 1997 (PMID 9300182).

- 10) Payson RA, **Chotani MA**, Chiu I-M. Regulation of a promoter of the fibroblast growth factor 1 gene in prostate and breast cancer cells. *J Steroid Biochem Molec Biol.* 66(3): 93-103; 1998 (PMID 9719443).
- 11) **Chotani MA**, Touhalisky K, Chiu I-M. The small GTPases Ras, Rac1 and Cdc42 transcriptionally regulate expression of human fibroblast growth factor 1. *J Biol Chem.* 275(39): 30432-30438; 2000 (PMID 10849427).
- 12) **Chotani MA**, Flavahan S, Mitra S, Daunt D, Flavahan NA. Silent α_{2C} -adrenergic receptors enable cold-induced vasoconstriction in cutaneous arteries. *Am J Physiol. Heart Circ Physiol.* 278:H1075-H1083; 2000 (PMID 10749700).
- 13) Su B, Mitra S, Gregg H, Flavahan S, **Chotani MA**, Goldschmidt-Clermont PJ, Clark KR, Flavahan NA. Redox regulation of vascular smooth muscle cell differentiation. *Circ Res.* 89:39-46; 2001 (PMID 11440976).
- 14) Jeyaraj SC, **Chotani MA**, Mitra S, Gregg HE, Flavahan NA, Morrison KJ. Cooling evokes redistribution of α_{2C} -adrenoceptors from Golgi to plasma membrane in transfected human embryonic kidney 293 cells. *Mol Pharmacol.* (Accelerated Communication) 60:1195-1200; 2001 (PMID 11723226).
- 15) ***Chotani MA**, Mitra S, Su BY, Flavahan S, Eid AH, Clark KR, Montague C, Paris H, Handy D E, Flavahan NA. Regulation of α_2 -adrenoceptors in human vascular smooth muscle cells. *Am J Physiol. Heart Circ. Physiol.* [special "Translational Physiology" series article] 286: H59-H67; 2004 (PMID 12946937).
- 16) ***Chotani MA**, Mitra S, Eid AH, Han SA, Flavahan NA. Distinct cyclic AMP signaling pathways differentially regulate α_{2C} -adrenoceptor expression: role in serum induction in human arteriolar smooth muscle cells. *Am J Physiol. Heart Circ Physiol.* [special "Translational Physiology" series article] 288: H69-H76; 2005 (PMID 15345481).
- 17) Eid A H, Maiti K, Mitra S, **Chotani MA**, Flavahan S, Bailey SR, Thompson-Torgerson CS, Flavahan NA. Estrogen increases smooth muscle expression of α_{2C} -adrenoceptors and cold-induced constriction of cutaneous arteries. *Am J Physiol. Heart Circ Physiol.* 293: H1955-H1961; 2007 (PMID 17644575).
- 18) Bayoumi MM, Alkheraije KA, El-Sayed O, Wisel S, Sarker K, **Chotani MA**, Zweier JL, Nuovo G, Goldschmidt-Clermont PJ, Hassanain H. Vascular hypertrophy and hypertension caused by transgenic overexpression of profilin 1. *J Biol Chem.* 282:37632-37639; 2007 (PMID 17942408).
- 19) Eid AH[†], **Chotani MA**[†], Mitra S, Miller TJ, Flavahan NA. Cyclic AMP acts through Rap1 and JNK signaling to increase expression of cutaneous smooth muscle α_{2C} -adrenoceptors. *Am J Physiol. Heart Circ Physiol.* 295: H266-H272; 2008 (PMID 18487435).
- 20) Mihai C, **Chotani M**, Elton TS, Agarwal G. Mapping of DDR1 distribution and oligomerization on the cell surface by FRET microscopy. *J Mol Biol.* 385: 432- 445; 2009 (PMID 19007791).

- 21) Jeyaraj SC, Unger NT, Eid AH, Mitra S, El-Dahdah NP, Quilliam LA, Flavahan NA, ****Chotani MA**. Cyclic AMP-Rap1A Signaling Activates RhoA to Induce α_{2C} -Adrenoceptor Translocation to the Cell Surface of Microvascular Smooth Muscle Cells. *Am J Physiol. Cell Physiol.* 303: C499-C511; 2012 (PMID 22621783).

This article is accompanied by an editorial by Martin C. Michel and Paul A. Insel: Michel MC, Insel PA. *Can you blame cold feet on Epac (and Rap1A)?* Focus on "Cyclic AMP-Rap1A signaling activates Rho to induce α_{2C} -Adrenoceptor Translocation to the Cell Surface of Microvascular Smooth Muscle Cells." *Am J Physiol Cell Physiol.* 303: C488-C489; 2012.

This article was included in "Editor's Picks" for summer 2012, and was highlighted in a press release by the American Physiological Society on July 31, 2012 (<http://www.the-aps.org/mm/hp/Audiences/Public-Press/For-the-Press/releases/12/29.html>),

and *HealthDay* news (<http://consumer.healthday.com/Article.asp?AID=667527>)

(which was picked up by MSN (icy feet, icy reception video), US News & World Report, Raynaud's Association, and TV channels).

- 22) Jeyaraj SC, Mitra S, Motawea HKB, Unger NT, Flavahan NA, ****Chotani MA**. Identification of a Novel α_{2C} -adrenoceptor Interaction with Filamin-2: Role in Translocation to the Cell Surface of Microvascular Smooth Muscle Cells. In Revision.

Invited Reviews

- 23) Jeyaraj SC, Unger NT, ****Chotani MA**. Rap1 GTPases: an emerging role in the cardiovascular. *Life Sciences (Molecular, Cellular and Functional Basis of Therapy)* 88: 645-652; 2011 (PMID 21295042).
- 24) **Chotani MA**, Flavahan NA. Intracellular α_{2C} -adrenoceptors: storage depot, stunted development or signaling domain? *Biochimica et Biophysica Acta-Molecular Cell Research*, 1813(8): 1495-1503; 2011 (PMID 21605601).

This collaborative effort with Johns Hopkins University includes a timely discussion and review of G protein coupled receptors that are preferentially retained within intracellular ER and Golgi compartments, and focuses primarily on α_{2C} -adrenoceptors as an example.

- 25) Flavahan, N.A., Flavahan, S., Mitra, S., **Chotani, M.A.** The Vasculopathy of Raynaud's Phenomenon and Scleroderma. In: *Rheum. Dis. Clin. North Am. (Scleroderma)* 29:275-291, White B., Guest Editor. W.B. Saunders Company, 2003.

Manuscripts in preparation

- 26) Jeyaraj SC, Unger NT, El-Dahdah NP, Sessler RJ, Zirwas M, Pleister A, Green-Church KB, McConnell B, ****Chotani MA**. Delocalization of endogenous A-kinase antagonizes the positive effects of Rap-Rho signaling in human microvascular smooth muscle cells. In Preparation.

- 27) Jeyaraj SC, Roof SA, Ziolo MT, Joshi MS, Quilliam LA, Bauer JA, ***#Chotani MA**. Electrophysiological abnormality in Rap1a GTPase deficient cardiac myocytes. In Preparation.

*Corresponding author

† Shared first authorship

#Senior author

Dissertation/Thesis

- **Chotani, M.A.** 1997. Cellular and molecular analysis of regulatory mechanisms of human Fibroblast Growth Factor 1 gene expression. Dissertation. The Ohio State University, Columbus, Ohio.
- **Chotani, M.A.** 1988. Use of ordered deletions in place of shotgun cloning, and dideoxy sequencing of the mouse VL30 gene cloned in the pUC119 plasmid vector. Senior Independent Thesis. The College of Wooster, Wooster, Ohio.

Submitted Abstracts

- Motawea HKB, Jeyaraj SC, Pawlowski M, Kloczkowski A, **#Chotani MA**. Cyclic AMP-Rap1A signaling mediates cell surface translocation of microvascular smooth muscle α_{2C} -adrenoceptors through the actin binding protein filamin-2. Experimental Biology 2013, Boston, MA.
- Randive R, Jeyaraj SC, **Chotani, MA**, Stewart, Jr., JA. Rap1a mediates extracellular matrix (ECM) remodeling through AGE/RAGE signaling in diabetes mellitus. Experimental Biology 2013, Boston, MA.

Published Abstracts

- Fidelibus R, Jeyaraj SC, Unger NT, Biesiadecki BJ, **#Chotani MA**. Peptide expression and purification to elucidate the mechanism of vascular α_{2C} -adrenoceptor translocation. Experimental Biology 2012, San Diego, CA (*FASEB J.* 26:870.8, 2012).
- Jeyaraj SC, Unger NT, Stewart Jr JA, **#Chotani MA**. Rap 1a small GTPase alters extracellular matrix (ECM) deposition in response to TGF- β 1. Experimental Biology 2012, San Diego, CA (*FASEB J.* 26:1133.4, 2012).
- Jeyaraj SC, Unger NT, El-Dahdah NP, Sessler RJ, Zirwas M, Pleister A, Green-Church KB, McConnell B, **#Chotani MA**. Delocalization of endogenous human microvascular smooth muscle A-kinase antagonizes the positive effects of Rap-Rho signaling on cell integrity and survival. AHA Scientific Sessions 2010, Chicago, IL (*Circulation* 2010; 122 (21 Supplement): A19886 (peer-reviewed)).
- Jeyaraj SC, Unger NT, El-Dahdah NP, Sessler RJ, Zirwas M, Pleister A, Green-Church KB, **#Chotani MA**. Analysis of cyclic AMP-coupled signature molecules in human micro vascular smooth muscle cells shows link to stress-associated proteins. *FASEB J.* 24: 870.1, 2010.

- Jeyaraj SC, Joshi MS, Huang H, Unger NT, El-Dahdah NP, Wold LE, Strauch AR, Elton TS, Quilliam LA, Bauer JA, **Chotani MA**. Electrophysiological abnormalities in mice with genetic ablation of Rap1a GTPase. *FASEB J.* 24: 867.3, 2010.
- **Chotani, M.A.**, Eid, A.H., Mitra, S., Flavahan, N.A. An arginine-rich region mediates *trans*Golgi retention of α_{2C} -adrenoceptors. Experimental Biology 2007 Symposium, Washington DC, April 28-May 2, 2007. *FASEB J.* 21 (6): A1210.
- **Chotani, M.A.**, Mitra, S., Eid, A.H., Flavahan, N.A. Rap1 and filamin-2 regulate subtype-specific, cell-surface delivery of α_2 -adrenoceptors. Featured Topic Session on *Receptor Biology: intracellular signaling and second messengers*, Experimental Biology 2007 Symposium, Washington DC, April 28-May 2, 2007. *FASEB J.* 21 (6): A1209.
- **Chotani, M.A.**, Mitra, S., Flavahan, N.A. Interaction with filamin2 enables translocation of α_{2C} -adrenoceptors to the plasma membrane of smooth muscle cells. Experimental Biology 2006, April 1-5, 2006, San Francisco, CA, *FASEB J.* 20 (5): A1176.
- **Chotani, M.A.**, Mitra, S., Eid, A.H., Miller, T.J., Flavahan, N.A. Rap1 GTPase stimulates translocation of α_{2C} -adrenoceptors from the *trans*Golgi to the plasma membrane. Experimental Biology 2006, April 1-5, 2006, San Francisco, CA, *FASEB J.* 20 (5): A1177.
- Eid A. H., Mitra S., **Chotani M.A.**, Miller T.J., Flavahan N. A. A novel Rap1 signaling pathway mediates increased expression of α_{2C} -adrenoceptors in human cutaneous vascular smooth muscle cells. Scientific Sessions 2005, American Heart Association meeting, November 13-16, 2005, Dallas, Texas, *Circulation* (supplement, October 25, 2005) 112: II-131 (abstract 718).
- **Chotani, M.A.**, Mitra, S., Flavahan, S., Flavahan, N.A. Distinct cyclic AMP signaling pathways differentially regulate α_{2C} -adrenoceptor expression in human arteriolar vascular smooth muscle cells. Scientific Sessions 2003, American Heart Association meeting, November 9-12, 2003, Orlando, Florida, *Circulation* (supplement IV, Oct 28, 2003) 108:100 (abstract 468).
- **Chotani, M.A.**, Jeyaraj, S.C., Mitra, S., Morrison, K.J., Flavahan, S., Flavahan, N.A. Induction of α_{2C} -adrenoceptors in human microvascular smooth muscle cells by cyclic AMP dependent, but A-kinase independent signaling. Experimental Biology 2003, American Society for Pharmacology & Experimental Therapeutics, San Diego, California (April 11-15, 2003). *FASEB J.* 17 (4): A214.
- Jeyaraj, S.C., **Chotani, M.A.**, Mitra, S., Flavahan, S., Flavahan, N.A., and Morrison, K.J. 2001. Cooling induces redistribution of α_{2C} -adrenergic receptors in HEK293 cells. *J. Vasc. Res.* 38 (S1), 14.
- Jeyaraj, S.C., **Chotani, M.A.**, Mitra, S., Flavahan, S., Gregg, H.E., Flavahan, N.A., and Morrison, K.J. 2001. Cold-induced redistribution of α_{2C} -adrenergic receptors. *FASEB J.* 15(4): A217.
- **Chotani, M.A.**, Mitra, S., Su, B.Y., Flavahan, S., Paris, H., Daunt, D.A., Handy, D.E., Clark, K.R. and Flavahan, N.A. Regulation of α_{2C} -adrenergic receptor expression in vascular smooth

muscle cells. Presented at the ASBMB/ASPET 2000 meeting, Boston, MA. *FASEB J. (Abstracts)* 14 (8):A1315, May 11, 2000, abstract 28.

- Morrison, K.J., **Chotani, M.A.**, Flavahan, S., Mitra, S., Gregg, H.E., Daunt, D. A. and Flavahan, N.A. α_{2C} -adrenoceptors and cold-induced vasospasm. Presented at the ASBMB/ASPET 2000 meeting, Boston, MA. *FASEB J. (Abstracts)* 14 (8):A1315, May 11, 2000, abstract 27.
- **Chotani, M.A.**, Flavahan, S., Mitra S., Daunt, D.A. and Flavahan, N.A. Silent α_{2C} -adrenergic receptors enable cold-induced vasoconstriction in cutaneous arteries: a mechanism for Raynaud's Phenomenon? Presented at the 72nd Scientific Sessions of the American Heart Association, Atlanta, Georgia, November 9, 1999, *Circulation (supplement)*, 100 (18):I-554, November 2, 1999, abstract 2922.
- **Chotani, M.A.**, Mitra, S., Su, B.Y., Flavahan, S., Paris, H., Daunt, D.A., Handy, D.E. and Flavahan, N.A. Microvascular smooth-muscle specific expression of α_{2C} -adrenergic receptor: role of oxidant stress and stress-activated protein kinase p38 in gene regulation. Presented at the 72nd Scientific Sessions of the American Heart Association, Atlanta, Georgia, November 10, 1999, *Circulation (supplement)*, 100 (18):I-848, November 2, 1999, abstract 4479.
- Myers, R.L., **Chotani, M.A.** and Chiu, I.-M. Transcriptional regulation of human FGF-1: potential interaction between positive and negative regulatory proteins. Poster presentation at the Keystone Symposia on Molecular Biology of the Endothelial Cell, January 16-23, 1994, (*J. Cell. Biochem*, Supplement 18A, abstract EZ 206, 324, 1994).
- **Chotani, M.A.**, Winkles, J.A. and Chiu, I.-M. Promoter switching of FGF-1 gene expression in vascular smooth muscle cells in response to serum and phorbol ester. Poster presentation at the Keystone Symposia on Inflammation, Growth Regulatory Molecules and Atherosclerosis, January 16-23, 1994, Keystone, Colorado, (*J. Cell. Biochem*, Supplement 18A, abstract E 203, 277, 1994).
- Hodgson, C.P., Fisk, R.Z., Hatzoglu, M., Arora, P., **Chotani, M.A.** and Hanson, R.W. Mouse retrovirus- like (VL-30) transposable element RNA is abundantly expressed in psi-2 helper cells, transferred to recipient rat hepatoma cells, and expressed in a dexamethasone-inducible fashion along with specifically vectored sequences: complete structure. Poster session for the 18 th Annual UCLA Symposia on Biotechnology and Human Genetic Predisposition to Disease, March 27 -April 7, 1989. (*J. Cell. Biochem*. Supplement 13D, abstract K415, 1989).

Unpublished Scholarly Presentations (local, national, international)

Local

- Fidelibus R, Jeyaraj SC, Unger NT, Biesiadecki BJ, Chalmers J, Wood B, **Chotani MA.** Elucidating the mechanism of vascular α_{2C} -adrenoceptor cell surface translocation. 17th Annual Denman Undergraduate Research Forum (May 9, 2012), The Ohio State University.
- Huang H, Joshi MS, Bauer JA, Wold LE, Strauch AR, Elton TS, Quilliam LA, **#Chotani MA.** Cardiac abnormalities in mice with genetic ablation of Rap1A GTPase. 2009 Research Day, The Research Institute at Nationwide Children's Hospital (oral competition finalist)

- Joshi MS, Bauer JA, Wold LE, Strauch AR, Elton TS, Quilliam LA, #**Chotani MA**. Cardiac abnormalities in mice with genetic ablation of Rap1A GTPase. *Third Annual Dorothy M. Davis Heart & Lung Research Institute Research Retreat Abstract Competition*, The Ohio State University Medical Center (October 21, 2008; award winning poster).
- Mihai, C., **Chotani, M.**, Iscru, D.F., Garbellini, D., Elton, T.S., Agarwal, G. Investigating DDR1 oligomerization at the single molecule level. Fifth Annual Ohio State University Medical Center Graduate & Postgraduate Research Day, March 30, 2006.
- Savla M., Sun P., Rathman J., **Chotani M.**, Mihai C., Agarwal G. DIP pen nanolithography: a novel approach to study lipid-protein interaction. Fourth Annual Ohio State University Medical Center Graduate & Postgraduate Research Day, March 31, 2005.
- Eid, A.H., **Chotani, M.A.**, Mitra, S., Flavahan, S., Flavahan, N.A. Estrogen increases α_{2C} -adrenoceptor expression in human microvascular smooth muscle cells. Third Annual Ohio State Medical Center Graduate & Postgraduate Research Day, April 1, 2004.
- Mihai, C., Vikram, D.S., **Chotani, M.A.**, Agarwal, G. Does glycosylation mediate discoidin domain receptor (DDR)-collagen interaction? Third Annual Ohio State Medical Center Graduate & Postgraduate Research Day, April 1, 2004.
- **Chotani, M.A.** and Chiu, I.-M. Functional analysis of human fibroblast growth factor 1 promoters shows linkage to Ras, Rac1, and Cdc42 signaling. Presented at the 9th Annual Ohio State University Molecular Biology Program Stone Laboratory Meeting, September 12-14, 1997, Gibraltar Island, Ohio.
- **Chotani, M.A.** and Chiu, I.-M. Cellular and molecular analysis of regulatory mechanisms of human fibroblast growth factor 1 gene expression. Poster session for the 23rd Annual ICSABER Society Graduate Research Forum, May 23, 1997, The Ohio State University, Columbus, Ohio.
- **Chotani, M.A.** Transforming growth factor- β 1 and heparin modulate gene expression of fibroblast growth factor-1: towards an understanding of the biological significance of alternate promoter usage by a growth factor gene. Presented at the Graduate Research Forum, The Ohio State University, April 22, 1995, Columbus, Ohio.
- **Chotani, M.A.** Heparin and oncogenic ras modulate gene expression of fibroblast growth factor-1: towards an understanding of the biological significance of alternate promoter usage by a growth factor gene. Presented at the Scott Falkenthal Memorial Graduate Student Colloquium, Department of Molecular Genetics, The Ohio State University, January 28, 1995, Columbus, Ohio.
- **Chotani, M.A.** Some aspects of FGF-1 gene expression. Presented at the Sixth Annual Ohio State University Molecular Biology Meeting, September 9-11, 1994, Stone Laboratory, Gibraltar Island, Ohio.
- **Chotani, M.A.** and Chiu, I.-M. Increased levels of FGF-1 mRNA in response to serum, phorbol ester, and TGF- β 1: identification of variant transcripts arising from alternate promoters. Poster

Session for the 20th Annual ICSABER Society Graduate Research Forum, May 10, 1994, The Ohio State University, Columbus, Ohio.

- **Chotani, M.A.** Gene expression of human fibroblast growth factor-1 (FGF-1) is modulated by alternate promoters in response to serum, PMA, and TGF- β 1. Presented at the Scott Falkenthal Memorial Graduate Student Colloquium, Department of Molecular Genetics, January 15, 1994, The Ohio State University, Columbus, Ohio.
- **Chotani, M.A.**, Winkles, J.A. and Chiu, I.-M. Identification and distribution of a novel human acidic fibroblast growth factor mRNA: a fourth variant having alternative 5' untranslated exon. Poster Session for the 19th Annual ICSABER Society Graduate Research Forum, May 5, 1993, The Ohio State University, Columbus, Ohio.
- **Chotani, M.A.** Characterization of a novel form of human aFGF mRNA. Presented at the Fourth Annual DNA Virus/Gene Expression Meeting, The Ohio State University, September 19-21, 1992, Stone Laboratory, Gibraltar Island, Ohio.

National

- Mihai, C., **Chotani, M.A.**, Elton, T.S., Agarwal, G. Does Collagen type I modulate oligomerization of DDR1? 51st Biophysical Society Meeting, Baltimore, Maryland, March 2007.
- Eid, A. H., Mitra, S., **Chotani, M.A.**, Flavahan, S., Flavahan, N.A. Estrogen increases α_{2C} -adrenoceptor expression in human microvascular smooth muscle cells. Experimental Biology 2005, April 2-6, San Diego, CA.
- **Chotani, M.A.**, Jeyaraj, S., Mitra, S., Morrison, K.J., Flavahan, S., Flavahan, N.A. Role of COX-2 and cyclic AMP in regulating expression of α_{2C} -adrenoceptors in human microvascular smooth muscle cells. Presented at the 10th International Symposium on Vascular Neuroeffector Mechanisms, Granlibakken, Lake Tahoe, California (July 12-15, 2002).
- Su, B.Y., Mitra, S., Gregg, H., Flavahan, S., **Chotani, M.A.**, Goldschmidt-Clermont, P.J. and Flavahan, N.A. Redox regulation of vascular smooth muscle differentiation. Presented at the First Conference on Arteriosclerosis, Thrombosis, and Vascular Biology, May 20-22, 2000, Denver, CO.
- Su, B.Y., Mitra, S., Gregg, H., Flavahan, S., **Chotani, M.A.**, Baldwin, W.M., Goldschmidt-Clermont, P.J. and Flavahan, N.A. Regulation of expression of the pro-apoptotic protein, BAD, by phenotypic modulation of vascular smooth muscle cells. Presented at the First Conference on Arteriosclerosis, Thrombosis, and Vascular Biology, May 20-22, 2000, Denver, CO.
- Chiu, I.-M., Myers, R.L., Payson, R.A., and **Chotani, M.A.** Differential expression of acidic fibroblast growth factor mRNA: Gene structure and distribution of four different aFGF transcripts. Poster Session for Keystone Symposia on Extracellular Matrix in Development and Disease in Breckenridge, Colorado, March 29-April 4, 1993.

- Payson, R.A., **Chotani, M.A.**, Myers, R.L., Harris, S.E., and Chiu, I.-M. Alternate 5'-untranslated exon/promoter usage renders tissue-specific transcriptional regulation of the human acidic fibroblast growth factor gene (aFGF). Poster Session for Keystone Symposia on Transcription: Factors, Regulation and Differentiation in Keystone, Colorado, January 17-24, 1993.
- Myers, R.L., Payson, R.A., **Chotani, M.A.**, and Chiu, I.-M. Tissue specific expression of multiple aFGF transcripts containing different 5' untranslated exons. Poster Session for Meeting of the American Society of Biochemistry, Molecular Biology and Biophysics in Houston, Texas, February 8-13, 1992.

International

- Piletz, J.E., Sarasua, M.M. and **Chotani, M.** Higher platelet internal membrane fluidity in Alzheimer's patients versus controls. Presented at the Second International conference on Alzheimer's disease and related disorders, July 19th 1990, Toronto, Canada.

Invited talks (local, national, international)

Local

- **Chotani, M.A.** Invited Works-in-Progress lecture, Department of Pathology, Ohio State University, October 6, 2011, 2-3 PM, Room 137 Hamilton Hall
"Mechanisms of vascular α_{2C} -adrenoceptor expression and mobilization"
- Integrated Biomedical Science Graduate Program (IBGP), and the Interdisciplinary Molecular, Cellular, & Developmental Biology (MCDB) Graduate Program, Ohio State University seminars (September 2, 2011, Graves Hall 1187, and September 13, 2011, 111 Parks Hall).
- **Chotani, M.A.** *"Regulated Cell surface delivery of α_{2C} -adrenoceptors"*: Invited session lecture 2009 Research Day, The Research Institute at Nationwide Children's Hospital, May 15th 2009 (CME approved presentation).

National

- **Chotani, M.A.**, Mitra, S., Eid, A.H., Flavahan, N.A. Rap1 and filamin-2 regulate subtype-specific, cell-surface delivery of α_2 -adrenoceptors. Featured Topic Session on *Receptor Biology: intracellular signaling and second messengers*, Experimental Biology 2007 Symposium, Washington DC, April 28-May 2, 2007.
- **Chotani, M.A.** Gene regulation of human fibroblast growth factor-1. Presented to The Clayton Foundation Laboratories for Peptide Biology, The Salk Institute for Biological Studies, August 11, 1995, La Jolla, California.

International

- **Chotani MA.** *Vascular α_{2C} -adrenoceptors: from skin punch biopsy to the culture dish.* Invited lecture, 2nd International Workshop-cum-Training Course on Molecular Medicine and Drug Research, Jan 5-7, 2009, Karachi, Pakistan (unable to attend due to other commitments; sent regrets).

- **Chotani MA.** Invited lecture, 4th International Symposium-Cum-Training Course on Molecular Medicine and Drug Research (MMDR-4), Jan 7-10, 2013, Karachi, Pakistan (unable to attend due to other commitments; sent regrets).
- **Chotani MA.** *Experimental and Computational Modeling Prediction Approaches To Elucidate Mechanism of Vascular α_{2C} -Adrenoceptor Translocation.* Invited session lecture, *Disease Related Proteins*, Zing Conference on Mathematical and Computational Medicine, December 1-December 5, 2012, Mayan Riviera at the Occidental Grand Xcaret Resort, Playa del Carmen, Mexico.
- **Chotani, M.A.** Expression of α_2 -adrenoceptors in human vascular smooth muscle cells. Presented to the Department of Biological and Biomedical Sciences, The Aga Khan University, College of Medicine, August 5, 2003, Karachi, Pakistan.

Acknowledged contributions to other published studies and dissertations:

Technical support

1. Piletz JE, Andorn AC, Unnerstall JR, Halaris A. Binding of [³H]-*p*-aminoclonidine to α_2 -adrenoceptor states plus a non-adrenergic site on human platelet plasma membranes. *Biochemical Pharmacology*, 1991 42(3): 569-584
2. Halbreich U, Piletz JE, Carson S, Halaris A, Rojansky N. Increased imidazoline and α_2 adrenergic binding in platelets of women with dysphoric premenstrual syndromes. *Biol Psychiatry* 1993. 34: 676-686.

Providing reagents for studies (NIH3T3 and human brain nuclear extracts)

3. Ritter LM, Bryans M, Abdo O, Sharma V, Wilkie NM. *MIP1 α* nuclear protein (MNP), a novel transcription factor expressed in hematopoietic cells that is crucial for transcription of the human MIP-1 α gene. *Mol Cell Biol* 1995, 15 (6): 3110-3118.

Dissertations

4. Ali H. Eid (The Ohio State University, 2004, Integrated Biomedical Science Graduate Program): *"Molecular regulation of vascular α_{2C} -adrenoceptors"*
5. Selvi C. Jeyaraj (The Ohio State University, 2007, Program in Molecular, Cellular & Developmental Biology): *"A role for the mRNA-stabilizing protein HUR in protection from cellular ATP depletion"*
6. Liantian Tian (Kent State University, 2010, School of Biomedical Sciences): *"G protein coupling and regulation of metabotropic glutamate receptor 6"*

Approved Institutional Research Protocols as Principal Investigator

1. IACUC, NCH (AR08-00072; active): *"Role of the Ras-related Rap1a GTPase in the cardiovascular"*
2. IACUC, Ohio State University (2006A0203; completed): *"Role of Rap GTPase in the cardiovascular"*
3. IRB, Ohio State University (2008H0061; completed): *"Novel endogenous mechanisms of microvascular smooth G protein coupled receptor (GPCR) regulation: role in health and in disease"*