

## BIOGRAPHICAL SKETCH

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NAME Cassis, Lisa A.	POSITION TITLE Professor		
eRA COMMONS USER NAME (credential, e.g., agency login) LISA_CASSIS			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
West Virginia University, Morgantown, WV	BS	05/80	Pharmacy
West Virginia University, Morgantown, WV	Ph.D.	05/84	Pharmacology
Univ. of Wurzburg, Wurzburg, W. Germany	Post-doc	05/85	Pharmacology
Univ. Of Virginia, Charlottesville, VA	Post-doc	03/88	Pharmacology

### A. Personal Statement

Research in my laboratory focuses on the renin-angiotensin system (RAS) in metabolic and cardiovascular diseases. Since our initial discovery in 1988 that adipocytes express a high level of mRNA abundance for angiotensinogen, the only known precursor to angiotensin II (AngII), my laboratory has been studying the regulation of and functional significance of an adipocyte RAS. These studies have been continuously funded by the NIH since 1988. In 1999, in collaboration with Dr. Alan Daugherty at the University of Kentucky, we made the initial observation that infusion of AngII to hyperlipidemic mice increases atherosclerosis and causes formation of abdominal aortic aneurysms (AAAs). In 2000, we published extensive characterization of AngII-induced AAAs in *The Journal of Clinical Investigation*, a paper that has been cited in excess of 340 times. Current research in my laboratory in this area focuses on mechanisms for sex differences in AAA formation. I am Project Director of a project within the University of Kentucky Superfund Basic Science Research Program focused on polychlorinated biphenyls (PCBs). Our research in this area focuses on PCB-induced diabetes, with an interest in the role of adipocyte aryl hydrocarbon receptors as mediators of inflammation and insulin resistance in adipocytes. I have extensive experience administering programs related to obesity and cardiovascular diseases as Director of a multidisciplinary graduate center focused on training nutritional scientists, Chair of a Department of Nutritional Sciences, Director of the NIH Center of Biomedical Research Excellence on Obesity and Cardiovascular Diseases, Chair of the Department of Molecular and Biomedical Pharmacology, and Director of an NIH T32 on Nutrition and Oxidative Stress.

### B. Positions and Honors

#### Positions and Employment

1980-1984	Pharmacist (part-time), Monongahela Hospital, Morgantown, WV
1984-1985	Alexander von Humboldt Postdoctoral Fellow; Department of Pharmacology, University of Wurzburg, Wurzburg, Germany
1985-1988	Postdoctoral Fellow; Dept. of Pharmacology, University of Virginia, Charlottesville, VA
1988-1994	Assistant Professor; College of Pharmacy, University of Kentucky, Lexington, KY
1994-2000	Associate Professor; College of Pharmacy, University of Kentucky, Lexington, KY
2000	Professor; College of Pharmacy, University of Kentucky, Lexington, KY
2003	Director and Chair, Graduate Center for Nutritional Sciences, University of Kentucky, Lexington, KY
2012	Chair, Department of Molecular and Biomedical Pharmacology

#### Professional Memberships and Honors

1986	National Research Service Award Postdoctoral Fellowship
1991	IBM Supercomputer Competition, First Place, Near IR Imaging of Atherosclerosis Lesions of Living Arteries, Lisa Cassis and Robert Lodder
1992	Research Career Development Award, NIH/LBI
1996-2003	National American Heart Association Grant Reviewer, Co-Chair
1997-2001	Pharmacology Study Section Member, NIH

- 2010 Associate Editor, Gender Medicine
- 2010 Leadership Council, Council of High Blood Pressure Research, American Heart Association
- 2010 College of CRS Reviewers, NIH
- 2011-2016 Standing member, Vascular Cell and Molecular Biology Study Section, NIH
- 2012 Women's Mentor of the Year, Council on Arteriosclerosis, Thrombosis, and Vascular Biology, American Heart Association
- 2012 Mentor of the year, Center for Clinical and Translational Sciences, University of Kentucky
- 2012 Council for High Blood Pressure Research Harriett Dustan Award for Excellence in Hypertension Research, American Heart Association

**C. Selected Peer-reviewed Publications** (Selected from >120 peer-reviewed publications)

**Most relevant to the current application**

1. **Cassis LA**, Saye J, Peach MJ. Location and regulation of rat angiotensinogen messenger RNA. *Hypertension* 11:591-6, 1988.
2. **Cassis LA**, Lynch KR, Peach MJ. Localization of angiotensinogen messenger RNA in rat aorta. *Circ Res* 62:1259-62, 1988.
3. Daugherty, A., Manning, M.W., & **Cassis, L.A.** (2000). Angiotensin II promotes rapid development of atherosclerotic lesions and aneurysm formation in apolipoprotein E-/-mice. *Journal of Clinical Investigation* 105(11), 1605-1612. PMID: PMC300860
4. Henriques TA, Huang J, D'Souza SS, Daugherty A, **Cassis LA**. Orchidectomy, but not ovariectomy, regulates angiotensin II-induced vascular diseases in apolipoprotein E deficient mice. *Endocrinology* 145:3866-72, 2004.
5. Daugherty A, Rateri DL, Lu H, Inagami T, **Cassis LA**. Hypercholesterolemia stimulates angiotensin peptide synthesis and contributes to atherosclerosis through the AT1A receptor. *Circulation* 110:3849-57, 2004.
6. **Cassis LA**, Rateri DL, Lu H, Daugherty A. Bone marrow transplantation reveals that recipient AT1a receptors are required to initiate angiotensin II-induced atherosclerosis and abdominal aortic aneurysms. *Arterioscler Thromb Vasc Biol* 27:380-6, 2006.
7. Henriques T, Zhang X, Yiannikouris FB, Daugherty A, **Cassis LA**. Androgen increases AT1a receptor expression in abdominal aortas to promote angiotensin II-induced AAAs in apolipoprotein E-deficient mice. *Arterioscler Thromb Vasc Biol* 28(7):1251-6, 2008, PMID: PMC2757112.
8. Police, S.B., Thatcher, S.E., Charnigo, R., Daugherty, A., & **Cassis, L.A.** Obesity promotes inflammation in periaortic adipose tissue and angiotensin II-induced abdominal aortic aneurysm formation. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 29(10), 1458-1464, 2009. PMID: PMC2753598
9. Thatcher SE, Zhang X, Howatt DA, Lu H, Gurley SB, Daugherty A, **Cassis LA**. Angiotensin converting enzyme 2 deficiency in whole body or bone marrow-derived cells increases atherosclerosis in low density lipoprotein receptor-/- mice. *Arterioscler Thromb Vasc Biol* 31:758-65, 2011. PMID: PMC3086633.
10. Yiannikouris F, Karounos M, Charnigo R, English VL, Rateri DL, Daugherty A, **Cassis LA**. Adipocyte-specific deficiency of angiotensinogen decreases plasma angiotensinogen concentration and systolic blood pressure in mice. *Amer J Physiol* 302:R244-51, 2012. PMID: PMC3349391. \*An invited editorial accompanied this publication.
11. Gupte M, Thatcher Se, Boustany-Kari CM, Shoemaker R, Yiannikouris F, Zhang X, Karounos M, **Cassis LA**. Angiotensin converting enzyme 2 contributes to sex differences in the development of obesity hypertension in C57BL/6 mice. *Arterioscler Thromb Vasc Biol* 32:1392-6, 2012. PMID: PMC3355213.
12. Zhang X, Thatcher SE, Rateri DL, Bruemmer D, Charnigo R, Daugherty A, **Cassis LA**. Transient exposure of neonatal female mice to testosterone abrogates the sexual dimorphism of abdominal aortic aneurysms. *Circ Res* 110:e73-85, 2012. PMID: PMC3518797.
13. Putnam K, Batifoulier-Yiannikouris F, Bharadwaj KG, Lewis E, Karounos M, Daugherty A, **Cassis LA**. Deficiency of angiotensin type 1a receptors in adipocytes reduces differentiation and promotes hypertrophy of adipocytes in lean mice. *Endocrinology* 153:4677-86, 2012. PMID: PMC3512029.
14. Yiannikouris F, Gupte M, Putnam K, Thatcher S, Charnigo R, Rateri DL, Daugherty A, **Cassis LA**. Adipocyte deficiency of angiotensinogen prevents obesity-induced hypertension in male mice. *Hypertension* 60:1524-30, 2012. PMID: PMC3517298. \*An invited editorial will accompany this publication.

Program Director/Principal Investigator (Last, First, Middle)

15. Baker NA, Karounos M, English V, Fang J, Wei Y, Stromberg A, Sunkara M, Morris AJ, Swanson HI, **Cassis LA**. Coplanar polychlorinated biphenyls impair glucose homeostasis in lean C57BL/6 mice and mitigate beneficial effects of weight loss on glucose homeostasis in obese mice. *Environ Health Persp*, epub ahead of press, 2012. PMID: 23099484. \*An invited editorial will accompany this publication.

#### D. Research Support

##### Ongoing Research Support

- |                                                                                                                                                                                                                                                               |                           |                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|---------------------|
| R01 HL073085-09<br>Angiotensin: A Link Between Obesity and Hypertension<br>The proposed studies will determine the role of adipose-derived angiotensin peptides in obesity-hypertension.<br>Role: PI                                                          | Cassis (PI)               | 07/01/09 – 06/30/13 |
|                                                                                                                                                                                                                                                               |                           |                     |
| P42 ES007380-16<br>The Impact of Obesity on PCB Toxicity<br>The proposed studies will define the role of polychlorinated biphenyls (PCBs) on angiotensin II-induced vascular diseases.<br>Role: Co-Investigator, PI – Project 4                               | Hennig (PI)               | 04/01/08 – 03/31/13 |
|                                                                                                                                                                                                                                                               |                           |                     |
| 8P20GM103527-05<br>Center of Research in Obesity and Cardiovascular Disease<br>The proposed research will develop a center for the study of obesity and cardiovascular disease, and consists of 5 junior investigators and mentors.<br>Role: Program Director | Cassis (Program Director) | 09/08/08 – 06/30/13 |
|                                                                                                                                                                                                                                                               |                           |                     |
| R01 HL107326-01A1<br>Sex differences in angiotensin II-induced vascular diseases<br>The proposed research will investigate the relative role of sex hormones versus sex chromosomes as mediators of increased aneurysm susceptibility in male mice.           | Cassis (PI)               | 04/01/12 - 03/31/16 |
|                                                                                                                                                                                                                                                               |                           |                     |
| 5P30HL101300-02<br>Biomedical Research Core Center on Fetal Programming                                                                                                                                                                                       | Cassis (PI)               | 09/30/09 – 08/31/13 |