

CURRICULUM VITAE

Andrea I. Doseff, Ph.D.

Present Address:

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Languages: Fluent in English, Spanish and French

Education:

1991-1996 Ph.D., Genetics. Cold Spring Harbor Laboratory and State University of New York at Stony Brook, New York.
Thesis: "The *LAS1* gene and the Role of SIT4 Phosphatase in Budding and Cell Morphology". Advisor: Dr. Kim Arndt.
1987-1989 Graduate Student. Center for Plant Ecophysiology, Buenos Aires, Argentina.
1987 Bachelor in Sciences, Biology. Faculty of Science, University of Buenos Aires, Argentina.

Professional Experience

July 2002- Assistant Professor, Department of Molecular Biology and Department of Internal Medicine, Heart and Lung Research Institute, The Ohio State University.
1998-2002 Research Scientist, Department of Internal Medicine, Heart and Lung Research Institute, The Ohio State University. Mentor Dr. Mark Wewers
1996-1998 Post-Doctoral Research Fellow with Dr. Yuri Lazebnik
Cold Spring Harbor Laboratory, Cold Spring Harbor, New York.
1989-1990 Research Associate with Dr. Venkatesan Sundaresan
Cold Spring Harbor Laboratory, Cold Spring Harbor, New York.

Teaching Experience

2002- Immunology Review Seminars. Department of Internal Medicine. Ohio State University
1990-1991 Teaching Assistant. Biology 101. State University of New York at Stony Brook, New York.
1986-1989 Teaching Assistant. a) Introductory Molecular Biology, b) Plant Physiology, c) Invertebrates, and d) Botany. Faculty of Sciences, University of Buenos Aires, Argentina.

Honors and Academic Awards

- 1996-1998 NIH Training Grant Postdoctoral Fellow.
1988-1989 Argentine National Research Council (CONICET) Graduate Fellow.

Research Funding

- * Bremen Foundation Award. Chemotatic molecules released by apoptotic cells. Principal Investigator: M.D. Wewers. Co-principal Investigator: A.I. Doseff, 03/01/00-03/01/02, \$50,000.
- * American Cancer Society. Regulation of caspase-3 activity by phosphorylation. Principal Investigator: A.I. Doseff, 01/01/00-12/01/01, \$15,000.
- * The Ohio State University, College of Medicine, Seed Grant. The anti-inflammatory cytokine IL-4 induces apoptosis of activated monocytes. Principal Investigator: A.I. Doseff, 04/01/01-05/01/02, \$9,000.
- * American Heart Association. Award was obtained but declined due to overlap with other grants. Principal Investigator: A.I. Doseff, 7/01/2001-08/01/2003, \$50,000.
- * American Lung Association. Role of caspase-3 regulation in human monocyte apoptosis. Principal Investigator: A.I. Doseff, 7/01/2001-08/01/2003, \$50,000.
- * National Institutes of Health. Regulation of macrophage interleukin-1 β production. Principal Investigator: M.D. Wewers. Co-principal Investigator: A.I. Doseff, 12/01/01-11/30/06, \$1,658,719.

Research Interests:

Molecular bases of cancer and cancer therapy. Relationships between cell division, cell death and oncogenesis. Regulation of programmed cell death and the potential to manipulate cell survival in cancer cells and during inflammation. Relationships between molecules involved in cell death and in inflammation and their signal transduction pathways. Role of inflammatory and anti-inflammatory cytokines in the modulation of cell death, survival and differentiation. Role of oxidants in cell death of primary cells. Therapies for the treatment of cancer, inflammation and autoimmune diseases.

Peer Reviewed Publications:

1. **Doseff, A.I.**, Bourgeois, T., and Wewers, M.D. The anti-inflammatory cytokine IL-4 induces apoptosis of stimulated monocytes by activating the caspase cascade. (submitted for publication).
2. Graham, M.M., Galloway, M.F., **Doseff, A.I.**, Nowicki, P.T., Sen, C.K and Marsh, C.B. The presentation of nitric oxide regulates monocyte life and death through effects on caspase-9 and caspase-3 activation. (submitted for publication).
3. **Doseff, A.I.**, and Wewers, M.D. Human caspase-3 is a phosphoprotein and associates with a kinase activity regulated during spontaneous monocyte apoptosis. (submitted for publication).
4. Rovin, B.H., Wilmer, W.A., Lu, L., **Doseff, A.I.**, Dixon, C., Kotur, M., and Hilbelink, T. (2002). The cyclopentenone prostaglandin 15-deoxy-^{12,14}-prostaglandin J₂ regulates mesangial cell proliferation and death. *Kidney Intern.* (in press).

5. Coulter, K.R., Sweeney, P., **Doseff, A.I.**, Wang, Y., Marsh, C.B, Wewers, M.D., Knoell, D.L. (2002). Opposing effect by cytokines on Fas-mediated apoptosis in A549 lung epithelial cells. *Am. J. Resp. Cell and Mol. Biol.* **26**: 58-66.
6. Goyal, A., Wang, Y., Graham, M.M., **Doseff, A.I.**, Bhatt, N.Y., and Marsh, C.B. (2002). Monocyte survival factors induce Akt activation and suppress caspase-3. *Am. J. Resp. Cell and Mol. Biol.* **26**: 224-230.
3. Fahy, R.J.*, **Doseff, A.I.***, and Wewers, M.D. (1999). Spontaneous human monocyte apoptosis utilizes a caspase-3 dependent pathway which is blocked by endotoxin and is independent of caspase-1. *J. Immunol.* **163**: 1755-1762.
4. Kirsch, D.G., **Doseff, A.I.**, Chau, B.N., Lim, D., Souza-Pinto, N.C., Hansford, R., Kastan, M.B., Lazebnik, Y.A., and Hardwick, J.M. (1999). Caspase-3-dependent cleavage of Bcl-2 promotes release of cytochrome c. *J. Biol. Chem.* **274**: 21155-21161.
5. Kelly, T., Graham, M., **Doseff, A.I.**, Pommerantz, R.W., Lau, S.M., Ostrowski, M.C., Franke, T.M., and Marsh, C. B. (1999). Macrophage colony-stimulating factor promotes cell survival through Akt/protein kinase B. *J. Biol. Chem.* **274**: 26393-26398.
6. Nestler. H.P., and **Doseff, A.I.** (1997). A two dimensional, diagonal SDS-PAGE technique to screen for proteases substrates in protein mixtures. *Anal. Biochem.* **251**: 122-124.
7. **Doseff, A.I.**, and Arndt, K.T. (1995). Las1 is an essential nuclear protein involved in morphogenesis and cell surface growth. *Genetics* **141**: 857-871.
8. **Doseff, A.I.**, Martienssen, R., and Sundaresan, V. (1991). Somatic excision of the *Mu1* transposable element of maize. *Nucl. Acids Res.* **19**:579-584.
9. Barneix, A.J., **Doseff, A.I.** and Rodgers, C.O. (1989). Nitrate reductase activity in Argentine wheat cultivars. *Cereal Research Comm.* **16**: 269-272.

* Indicates shared first authorship

In preparation:

10. **Doseff, A.I.**, Fahy, R.J, Sanckatar, O., and Wewers, M.D. Biochemical dissection of a signal transduction cascade leading to caspase activation during programmed cell death in human monocyte apoptosis.
11. **Doseff, A.I.**, Baker, J., Wewers, M.D. Caspase-3 activation requires an autocatalytic step.

Meeting Presentations and Invited Seminars:

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| 2002 | Doseff, A.I.* , Sancaktar, O. Waggoner, A.N.and Wewers, M.D. Caspase-3 is a phosphoprotein that associates with and is phosphorylated selectively by a PKC isoform during monocyte lifespan. (Oral presentation). American Thoracic Society International Conference, Atlanta, GO. |
| 2002 | Parker-Barnes, Doseff, A.I. , and Wewers, M.D. MAIL gene (I?B?) is rapidly induced by LPS in monocytes but not in alveolar macrophages. (Poster). American Thoracic Society International Conference, Atlanta, GO. |

- 2002 Matthews, N., **Doseff, A.I.**, Sun, H. Davuluri, V.R. A bioinformatic approach to identifying new human apoptotic markers. (Poster). Denman, Undergraduate Research Forum, Ohio State University, Columbus, OH.
- 2002 Guo, W., Kim, H-J, **Doseff, A.I.**, and Wewers, M.D. Cardiak is a constitutively expressed in monocytes and interacts transiently with caspase-1 after endotoxin. (Poster). FASEB. New Orleans, LO.
- 2002 Sancaktar, O., **Doseff, A.I.**, and Wewers, M.D. The apoptotic machinery of monocytes is halted until caspase-3 is activated. (Poster). Landacre Ohio State University, Columbus, OH.
- 2002 Guo, W., Kim, H-J, **Doseff, A.I.**, and Wewers, M.D. Cardiak is a constitutively expressed in monocytes and interacts transiently with caspase-1 after endotoxin. (Poster). Keystone Symposia: Innate Immunity: evolution and link to adaptive immunity. Keystone, CO.
- 2001 **Doseff, A.I.***, Bourgeois, T., and Wewers, M.D. IL-4 induces apoptosis of activated monocytes through a caspase-dependent pathway. (Oral presentation). American Thoracic Society International Conference, San Francisco, CA.
- 2001 Goyal, A., Graham, M.M., **Doseff, A.I.** and Marsh, C.B. Monocyte survival induced by inflammatory cytokines and growth factors results from suppression of caspase-3 activity in a PI 3-kinase dependent manner. (Poster). American Thoracic Society International Conference, San Francisco, CA.
- 2001 Rovin, B.H., Wilmer, W. A., Lu, L., Dixon, C., **Doseff, A.I.**, and Hilbelink, T. The cyclopentenone prostaglandin 15-deoxy- $\gamma^{12,14}$ -PGJ₂ (15dPGJ₂) regulates human mesangial cell (HMC) proliferation and survival. ASN/ISN World Congress of Nephrology. San Francisco, CA.
- 2001 **Doseff, A.I.***, and Wewers, M.D. (Oral presentation). Internal Medicine Fellows Day. Ohio State University, Columbus, OH.
- 2001 Graham, M.M., **Doseff, A.I.**, Goyal, A., Nowicki, P. T., and Marsh, C.B. Nitric oxide has a dual role in monocyte apoptosis via caspase-3 and the AKT-dependent pathway. (Poster). FASEB. Orlando, FL.
- 2001 Graham, M.M., **Doseff, A.I.**, Goyal, A., Nowicki, P. T., and Marsh, C.B. Nitric oxide has a dual role in monocyte apoptosis via caspase-3. (Poster). Research Conference Pathology Department Ohio State University, Columbus, OH.
- 2001 **Doseff, A.I.*** Molecular Biology and Cancer Genetics Program (Invited speaker). Ohio State University, Columbus, OH.
- 2001 **Doseff, A.I.***, and Wewers, M.D. Caspase-3 is a phosphoprotein and associates with a kinase that is modulated during monocyte activation and spontaneous monocyte apoptosis. (Poster). Keystone Symposia: Macrophage activation and deactivation: links between innate and acquired immunity and interfaces between innate and adaptive immunity. Keystone, CO.
- 2000 **Doseff, A.I.*** Caspases: regulating by proteolysis the apoptotic cascade. (Invited plenary speaker: Postgraduate course on regulation and function of apoptosis in lung biology). American Thoracic Society International Conference, Toronto, Canada.
- 2000 Fahy, R.J., **Doseff, A.I.*** and Wewers, M.D. Caspase activity in monocyte apoptosis. (Poster). American Thoracic Society International Conference, Toronto, Canada.

- 2000 **Doseff, A.I.**, *, Sadler, P.M. and Wewers, MD. Caspase-3 phosphorylation and its role in monocyte apoptosis. (Oral presentation). American Thoracic Society International Conference, Toronto, Canada.
- 2000 Bourgeois, T.A.*, Wewers, M.D. and **Doseff, A.I.** Dissecting the killing caspase cascade in human monocytes. (Poster). R.J. and M.D. Denman, Undergraduate Research Forum, Ohio State University, Columbus, OH.
- 1999 **Doseff, A.I.***, Fahy, R.J. and Wewers, M.D. Spontaneous monocyte apoptosis and endotoxin protection are dependent on caspase-3 and do not require caspase-1 activity. (Poster). FASEB, Washington, D.C.
- 1999 Coulter, K.R.*, **Doseff, A.I.**, and Knoell, D.L. Lung epithelial cells constitutively express caspase activity which is augmented by IL-1 and INF-?. (Oral presentation). American Thoracic Society Conference. San Diego, CA.
- 1997 **Doseff, A.I.***, Soengas, M.S., Lowe, S., and Lazebnik, Y. Delineating the caspase cascade by caspase depletion. (Oral presentation). Meeting on Programmed Cell Death. Cold Spring Harbor Laboratory, N.Y.
- 1995 **Doseff, A.I.***, and Arndt, K. Genetic screen to isolate genes involved in the function of SIT-4 phosphatase. (Poster). Meeting on Cell Cycle. Cold Spring Harbor Laboratory, N.Y.

* Indicates presenter

Membership and Professional Activities

American Lung Association.

American Thoracic Society International Conference. Organizational Committee, Assembly on Allergy, Immunology and Inflammation.

American Thoracic Society International Conference. Organizational Committee All Programs, General Assembly.

Reviewer for Scientific Journals

Cell Death and Differentiation, Journal of Leukocyte Biology, Blood.

Student Education

Kolattukudy, S. 6/01/1999-15/08/1999 and 6/01/2000-8/01/2000. High School Student. Currently Student at O.S.U.

Bourgeois, T. 12/01/99-8/20/2000. Honor Biochemistry. Currently at O.S.U. Dentist School.

Waggoner, A. 6/01/2001-6/02/2002. Honor Biology. Accepted into MCDB, OSU Ph.D. Program.

Elkhatib, I. 4/01/2001-present. Biology student.

Matthews, N. 9/01/2001-present. Computer Sciences student.

Sancaktar, O. 8/01/2000-present. Honor Engineering. Currently at O.S.U. Medical School. Awarded 2002 O.S.U.-CCC Summer Internship Program and The Samuel J. Roesler Research Scholarship. Role of Fas Receptor in Spontaneous Monocyte Apoptosis.