

BIOGRAPHICAL SKETCH

NAME Daria Mochly-Rosen eRA COMMONS USER NAME: mochlyrosen.daria	POSITION TITLE Professor
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EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Tel Aviv University, Tel Aviv, Israel	B.S.	1977	Life Sciences
The Weizmann Institute of Science, Rehovot, Israel	Ph.D.	1983	Chemical Immunology

A. POSITIONS AND HONORS

Positions and Employment:

1983-1985	Postdoctoral Fellow, Dept. of Biochemistry University of California, Berkeley
1986-1992	Fellow, Adjunct Assistant and Associate Professor, and Associate Professor in residence, Depts of Pharmacology & Neurology, Gallo Research Center, University of CA, San Francisco
1993-2000	Associate Professor, Dept of Molecular Pharmacology, Stanford University School of Medicine
2001-present	Professor, Chairman (until 2006), Department of Molecular Pharmacology
2003-present	The George D. Smith Professor in Translational Medicine
2006-present	Senior Associate Dean for Research, Stanford University School of Medicine

Other Experience and Professional Memberships:

1988- present	Member, American Society for Biochemistry and Molecular Biology
1993- present	Member, Neuroscience Program, Stanford University School of Medicine
1994	Burroughs Wellcome Foundation Visiting Professor in the Medical Sciences
1996- present	Member, Human Biology Program, Stanford University School of Medicine
1996- present	Member, Research Society on Alcoholism (RSA)
1996- present	Affiliated Member of The Ernest Gallo Clinic and Research Center, UC, San Francisco
1998- present	Member, Cancer Biology Program, Stanford University, School of Medicine
2002- present	Member, Cardiovascular Institute, Stanford University School of Medicine
2006- present	Member, Peer Review Advisory Committee, National Institutes of Health

Honors:

1982	The Feinberg Graduate School Scholar Prize, Weizmann Institute of Science
1983-1985	The Weizmann International Postdoctoral Fellowship
1990-1992	Basil O'Connor Scholar Research Award
1993-1995	American Cancer Society Research Award
1996-2001	The Reed-Hodgson Professor in Human Biology
2001	Founding Fellow of the International Society for Heart Research (ISHR)
2001	Fellow, Council on Basic Cardiovascular Sciences of the American Heart Association, AHA
2003-present	The George D. Smith Professor in Translational Medicine
2004-present	Professor, by courtesy, Department of Neurosurgery, Stanford University School of Medicine

Patents (related to the proposed study):

1. US6165977 MOCHLY-ROSEN D:
"Isozyme-specific activators of protein kinase C methods and composition".
2. US60/247, 830 MOCHLY-ROSEN D:
"Peptide use as a drug".
3. US66/262, 060 MOCHLY-ROSEN D:
"Activator and Inhibitor peptides of ϵ PKC and δ PKC, conjugates, thereof and method of treating ischemia".

B. SELECTED PEER-REVIEWED PUBLICATIONS (from over 134):

MOCHLY-ROSEN D: Localization of protein kinases by anchoring proteins: A theme in signal transduction. *Science* 268:247-251, 1995.

Ron D, Luo J, and MOCHLY-ROSEN D: C2 region-derived peptides inhibit translocation and function of protein kinase C *in vivo*. *J. Biol. Chem.* 270:24180-24187, 1995.

Johnson JA, Gray MO, MOCHLY-ROSEN D: A protein kinase C inhibitor as an isozyme-selective antagonist of cardiac function. *J. Biol. Chem.* 271:24962-24966, 1996.

- Johnson JA, Gray MO, Karliner JS, and MOCHLY-ROSEN D: An improved permeabilization protocol for the introduction of peptides into cardiac myocytes: application to protein kinase C. **Circ. Res.** 79:1086-1099, 1996.
- Zhang Z-H, Johnson JA, El-Sherif N, MOCHLY-ROSEN D, and Boutjdir M: C2 region-derived peptides of β -protein kinase C regulate cardiac Ca^{2+} channels. **Circ. Res.** 80:720-729, 1997.
- Csukai M, Chen C-H, de Matteis MA, and MOCHLY-ROSEN D: The coatomer protein β' cop, a selective binding protein (RACK) for protein kinase $\text{C}\epsilon$. **J. Biol. Chem.** 272:29200-29206, 1997.
- Gray MO, Karliner JS, and MOCHLY-ROSEN D: A selective ϵ -protein kinase C antagonist inhibits protection of cardiac myocytes from hypoxia-induced cell death. **J. Biol. Chem.** 272:30945-30951, 1997.
- MOCHLY-ROSEN D, Gordon AS: Anchoring proteins for PKC: a means for isozyme selectivity. **FASEB J.** 2:35-42, 1998.
- Souroujon M and MOCHLY-ROSEN D: Peptide modulators of protein-protein interactions in intracellular signaling; focus on protein kinases. **Nature Biotechnology** 16:919-924, 1998.
- Mackay K and MOCHLY-ROSEN D: An inhibitor of p38 mitogen-activated protein kinase protects neonatal cardiac myocytes from ischemia. **J. Biol. Chem.** 274:6272-6279, 1999.
- Dorn GW, Souroujon MC, Liron T, Chen C-H, Gray MO, Zhou HZ, Csukai M, Wu G, Lorenz JN, and MOCHLY-ROSEN D: Sustained *in vivo* cardiac protection by a rationally designed peptide that causes ϵ protein kinase C translocation. **Proc. Natl. Acad. Sci. USA** 96:12798-12803, 1999.
- MOCHLY-ROSEN D, Wu G, Hahn H, Osinska H, Liron T, Lorenz JN, Yatani A, Robbins J, and Dorn, GW: Cardioprotective effects of PKC ϵ : Analysis by *in vivo* mod of PKC ϵ translocation. **Circ. Res.** 86:1173-1179, 2000.
- Hu K, MOCHLY-ROSEN D, and Boutjdir M: Evidence for functional role of ϵ PKC isozyme in the regulation of cardiac Ca^{2+} channels. **Am. J. Physiol.** 279:H2658-2664, 2000.
- Mackay K and MOCHLY-ROSEM D: Localization, anchoring and functions of protein kinase C isozymes in the heart. **J. Mol. Cell. Cardiol.** 33:1301-1307, 2001.
- Mackay K and MOCHLY-ROSEN D: Arachidonic acid protects neonatal rat cardiac myocytes from ischemic injury through epsilon protein kinase C. **Cardiovasc. Res.** 50:65-74, 2001.
- Xiao, G-Q, Qu Y, Sun Z-Q, MOCHLY-ROSEN D and Boutjdir, M: Evidence for functional role of ϵ PKC isozyme in the regulation of cardiac Na channel. **Circulation.** 281: C1477-C1486, 2001.
- Chen L, Hahn H, Wu G, Chen C-H, Liron T, Schechtman D, Cavallaro G, Banci L, Guo Y, Bolli R, Dorn II GW, MOCHLY-ROSEN D: Opposing cardioprotective actions and parallel hypertrophic effects of δ and ϵ PKC. **Proc. Natl. Acad. Sci. USA.** 98:11114-11110, 2001
- Chen L, Wright LR, Chen CH, Oliver SF, Wender PA, MOCHLY-ROSEN D. Molecular transporters for peptides: delivery of a cardioprotective epsilon PKC agonist peptide into cells and intact ischemic heart using a transport system, R(7). **Chem. Biol.** 8:1123-1129, 2001.
- Banci L, Cavallaro G, Kheifets V, Mochly-Rosen D. Molecular dynamics characterization of the C2 domain of protein kinase C β . **J. Biol. Chem.** 277:12988-12997, 2002.
- Inagaki K, Hahn HS, Dorn GW, MOCHLY-ROSEN D: Additive protection of ischemic heart *ex vivo* by combined treatment with δ PKC inhibitor and ϵ PKC activator. **Circulation** 108: 869-875, 2003.
- Inagaki K, Chen L, Ikeno F, Lee FH, Imahashi K-I, Bouley DM, Rezaee M, Yock PG, Murphy E, MOCHLY-ROSEN D: Inhibition of delta protein kinase C protects against reperfusion injury of the ischemic heart, *in vivo*. **Circulation** 108: 2304-2306, 2003.
- Souroujon MC, Yao L, Chen H, Endemann G, Khaner H, Geeraert V, Schechtman D, Gordon AS, Diamond I, MOCHLY-ROSEN D: State specific monoclonal antibodies identify an intermediate state in epsilon protein kinase C activation. **J. Biol. Chem.** 279:17617-17624, 2004.
- Begley, R, Liron T, Baryza J, MOCHLY-ROSEN D, Biodistribution of intracellularly acting peptides conjugated reversibly to TAT47-57. **Biochem. Biophys. Res. Comm.** 318:949-954, 2004.
- Murriel CM, Churchill E, Inagaki K, Szweda LI, MOCHLY-ROSEN D: δ PKC activation induces apoptosis in response to cardiac ischemia and reperfusion damage: a mechanism involving BAD and the mitochondria. **J. Biol. Chem.** 279:47985-47991, 2004.
- Tanaka M, Terry RD, Mokhtari GK, Inagaki K, Koyanagi T, Kofidis T, MOCHLY-ROSEN D, Robbins RC: Suppression of graft coronary artery disease by a brief treatment with a selective ϵ PKC activator and a δ PKC inhibitor in murine cardiac allografts. **Circulation.** 110:194-199, 2004.
- Inagaki K, Begley R, Ikeno F, MOCHLY-ROSEN D: Cardioprotection by ϵ PKC activation from ischemia: continuous delivery and antiarrhythmic effect of an ϵ PKC-activating peptide. **Circulation.** 111:44-50, 2005.
- Churchill EN, Murriel CL, Chen CH, MOCHLY-ROSEN D, Szweda LI: Reperfusion-induced translocation of δ PKC to cardiac mitochondria prevents pyruvate dehydrogenase reactivation. **Circ. Res.** 97:78-85, 2005.
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Malhotra A, Begley R, Kang BP, Rana I, Liu J, Yang G, MOCHLY-ROSEN D, Meggs LG: PKC ϵ -dependent survival signals in diabetic hearts. **Am. J. Physiol. Heart Circ. Physiol.** 289:H1343-1350, 2005.

Tanaka M, Gunawan F, Terry RD, Inagaki K, Caffarelli AD, Hoyt G, Tsao PS, MOCHLY-ROSEN D, Robbins RC: Inhibition of heart transplant injury and graft coronary artery disease after prolonged organ ischemia by selective protein kinase C regulators. **J. Thorac. Cardiovasc. Surg.** 129:1160-1167, 2005.

Inagaki K, Begley R, Ikeno F, MOCHLY-ROSEN D: Cardioprotection by epsilon-protein kinase C activation from ischemia: continuous delivery and antiarrhythmic effect of an epsilon-protein kinase C-activating peptide. **Circulation.** 111:44-50, 2005.

Kheifets V, Bright R, Inagaki K, Schechtman D, MOCHLY-ROSEN D: Protein kinase C δ annexin V interaction: a required step in δ PKC translocation and function. **J. Biol. Chem.** 281:23218-23226, 2006.

Brandman R, Disatnik MH, Churchill E, MOCHLY-ROSEN D: Peptides derived from C2 domain of ϵ PKC modulate ϵ PKC activity and identify potential protein-protein interaction surfaces. **J. Biol. Chem.** 282:4113-4123, 2007.

Liron T, Chen L, Khaner H, Vallentin A, MOCHLY-ROSEN D: Rational design of a selective antagonist of ϵ PKC derived from the selective allosteric agonist, pseudo-RACK peptide. **J. Mol. Cell Cardiol.** 2007 (in press).

Ikeno F, Inagaki K, Rezaee M, MOCHLY-ROSEN D: Impaired perfusion after myocardial infarction is due to reperfusion-induced PKC-mediated myocardial damage. **Cardiovas. Res.** 2007 (in press)

C. RESEARCH SUPPORT

Ongoing Research Support:

N.I.H. R01 AA011147-10 (D. Mochly-Rosen) 08/01/04-05/31/09

"Mechanisms of ethanol-induced cardiac protection"

The major goal of this project is to assess the molecular basis and potential use of ethanol as an agent to protect the heart from ischemic damage. The work focuses on aldehyde dehydrogenase as a major mediator of ethanol-induced cardioprotection.

N.I.H. R01 HL076675-03(D. Mochly-Rosen) 04/01/04-03/31/09

"Hypertrophy, heart failure and PKC"

The major goal of this project is to determine whether PKC-regulating peptides can prevent, enhance or reduce cardiac remodeling and transition to heart failure. The work focuses on hypertension-induced heart failure.

N.I.H. R01 HL052141-11 (D. Mochly-Rosen) 08/01/03-06/30/07

"Protein kinase C isozymes in ischemic heart"

The major goal of this project is to determine the molecular mechanism by which inhibition of δ PKC in the heart protects from reperfusion injury and activation of ϵ PKC-mediated preconditioning. The proposal is a continuation of this project.

N.I.H R01 NS044350-04 (D. Mochly-Rosen) 02/01/03-01/31/08
(no cost extension through 01/31/08)

"Protein Kinase C Isozymes in Stroke - Therapeutic Target?"

The major goals of this project are to determine whether inhibition or activation of any of the any of the PKC isozymes can provide protection to the brain using rat model of stroke.

Completed Research Support (last 3 years):

0250204N AHA (D. Mochly-Rosen) 01/01/02-12/31/04

AHA Grant in Aid

"Assessing new therapeutics for cardiac ischemia using porcine model *in vivo*."

The major goals of this project were to assess whether a combination of treatment of PKC regulating peptides provides an enhanced therapeutic effect on the heart against ischemic damage in an *in vivo* pig model.
