

**BIOGRAPHICAL SKETCH**

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NAME Rozenfurt, Juan Enrique		POSITION TITLE	
eRA COMMONS USER NAME (credential, e.g., agency login) rozenfurt2		Distinguished Professor of Medicine	
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
University of Buenos Aires, Argentina	DVM	1965	Veterinary Medicine
University of Buenos Aires, Argentina	PhD	1971	Biological Chemistry
Princeton University, Princeton, NJ	Postdoctoral training	1972	Cell Biology

**A. Positions and Honors****Positions and Employment**

1971-72	Postdoctoral Fellow, Dept. of Biological Sciences, Princeton, NJ
1972-74	Research Fellow, Imperial Cancer Research Fund, London, UK
1974-77	Research Scientist, Imperial Cancer Research Fund, London, UK
1977-80	Senior Research Scientist, Imperial Cancer Research Fund, London, UK
1980-97	Principal Scientist; Head, Laboratory of Growth Regulation, Imperial Cancer Research Fund
1997-2006	Professor of Medicine; Director, Unit of Signal Transduction and Gastrointestinal Cancer, UCLA School of Medicine, Los Angeles, CA
2000-present	Chief of Research, Division of Digestive Diseases, UCLA School of Medicine, Los Angeles, CA
2002-present	Director, CURE: Digestive Diseases Research Center
2006-present	Distinguished Professor of Medicine; Director, Unit of Signal Transduction and Gastrointestinal Cancer, UCLA School of Medicine, Los Angeles, CA

**Other Experience and Professional Memberships**

Editorial Board Member; Journal of Biological Chemistry (1993-1998); Journal of Cellular Physiology; Cellular Signaling; Growth factors; Cellular Physiology and Biochemistry; Invasion and Metastasis; Journal of Molecular Signaling.

**Honors**

1990	Member of the European Molecular Biology Organization, (EMBO)
1991	Special Diploma, University of Buenos Aires, awarded for Outstanding Scientific Achievements
1993	Fellow of the Royal College of Pathologists, U.K.
1997	Honorary Professor of the University of Buenos Aires
2000	Ronald S Hirshberg Chair in Translational Pancreatic Cancer Research, UCLA School of Medicine.

**B. Selected peer-reviewed publications (in chronological order).**

(Publications selected from 441 peer-reviewed publications)

1. Valverde AM, Sinnott-Smith J, Van Lint J, **Rozenfurt** E. Molecular cloning and characterization of protein kinase D: a target for diacylglycerol and phorbol esters with a distinctive catalytic domain. Proc. Natl. Acad. Sci. USA 91: 8572-6, 1994.
2. Van Lint, J., Sinnott-Smith, J. and **Rozenfurt**, E. Expression and characterization of PKD: a phorbol ester and diacylglycerol-stimulated serine protein kinase. J. Biol. Chem. 270:1455-1461, 1995.
3. Zugaza, J.L., Sinnott-Smith, J., and **Rozenfurt**, E. Protein kinase D (PKD) activation in intact cells through a protein kinase C-dependent signal transduction pathway. EMBO Journal 15:6220-6230, 1996.

4. Casam assima A, **Rozengurt E.** Tyrosine phosphorylation of p130 Cas by bombesin, lysophosphatidic acid, phorbol esters, and platelet-derived growth factor. Signaling pathways and formation of a p130 Cas-Crk complex. *J. Biol. Chem.* 272:9363-70, 1997.
5. Zugaza, J.L. Waldron, R.T., Sinnett-Smith, J. and **Rozengurt, E.** Bombesin, Vasopressin, Endothelin, Bradykinin, and Platelet-derived Growth Factor Rapidly Activate Protein Kinase D through a Protein Kinase C-dependent Signal Transduction Pathway. *J. Biol. Chem.* 272:23952-23960, 1997.
6. Iglesias, T., Waldron, R.T. and **Rozengurt, E.** Identification of *in vivo* phosphorylation sites required for Protein Kinase D (PKD) activation. *J. Biol. Chem.* 273:27662-27667, 1998.
7. Salazar EP, **Rozengurt E.** Bombesin and platelet derived growth factor induce association of endogenous focal adhesion kinase with Src in intact Swiss 3T3 cells. *J. Biol. Chem.* 274:28371-8, 1999.
8. Waldron, R.T., Iglesias, T. and **Rozengurt, E.** The PH domain of Protein kinase D interacts preferentially with the Eta isoform of Protein kinase C. *J. Biol. Chem.* 274:9224-9230, 1999.
9. Matthews, S., Iglesias, T., **Rozengurt, E.** and Cantrell, D. Spatial and Temporal regulation of Protein Kinase D (PKD) in lymphocytes. *EMBO Journal* 19:2935-2945, 2000.
10. Waldron RT, **Rozengurt E.** Oxidative stress induces protein kinase D activation in intact cells involvement of Src and dependence on protein kinase C. *J. Biol. Chem.* 275:17114-17121, 2000.
11. Santiskulvong, C., Sinnett-Smith, J., and **Rozengurt, E.** EGF receptor function is required in late G<sub>1</sub> for cell cycle progression induced by bombesin and bradykinin. *Am. J. Physiol: Cell Physiol.* 281: C886-898, 2001.
12. Salazar E, **Rozengurt E.** Src family kinases are required for integrin-mediated but not for G protein-coupled receptor FAK autophosphorylation at Tyr-397. *J. Biol. Chem.* 276:17788-17795, 2001.
13. Rey O, Young SH, Cantrell D, **Rozengurt E.** Rapid Protein Kinase D Translocation in Response to G Protein-coupled Receptor Activation: Dependence on PKC. *J. Biol. Chem.* 276: 32616-32626, 2001.
14. Yuan J, Slice LW, **Rozengurt E.** Activation of protein kinase D (PKD) by signaling through Rho and the alpha subunit of the heterotrimeric G protein G13. *J. Biol. Chem.* 276:38619-38627, 2001.
15. Zhukova E, Sinnett-Smith J, **Rozengurt E.** Protein kinase D potentiates DNA synthesis and cell proliferation induced by bombesin, vasopressin or phorbol esters in Swiss 3T3 cells. *J. Biol. Chem.* 276:40298-40305, 2001.
16. Rey O, Sinnett-Smith J, Zhukova E, **Rozengurt E.** Regulated nucleocytoplasmic transport of protein kinase D in response to G protein-coupled receptor activation. *J. Biol. Chem.* 276: 49228-35, 2001.
17. Hurd, C., Waldron, R.T., **Rozengurt, E.** Protein Kinase D Complexes with C-Jun N-terminal Kinase Via Activation Loop Phosphorylation and Phosphorylates the C-Jun N-terminus. *Onco gene* 21: 2154-60, 2002
18. Chiu T, Wu SS, Santiskulvong C, Tangkijvanich P, Yee Jr. HF, **Rozengurt E.** Vasopressin-mediated Mitogenic Signaling in Intestinal Epithelial Cells. *Am. J. Physiol: Cell Physiol.* 282:C434-50, 2002.
19. Wu SS, Chiu T, **Rozengurt E.** Ang II and LP A induce Pyk2 tyrosine phosphorylation in intestinal epithelial cells: role of Ca<sup>2+</sup>, PKC, and Rho kinase. *Am. J. Physiol: Cell Physiol.* 282: C1432-44, 2002.
20. Wu, SV, **Rozengurt, N.** Yang, M, Young, SH, Sinnett-Smith, J. and **Rozengurt, E.** Expression of Bitter Taste Receptors of the T2R Family in the Gastrointestinal Tract and in Enteroendocrine STC-1 cells. *Proc. Natl. Acad. Sci. USA* 99:2392-2397, 2002.
21. Guha, S., Rey, O., **Rozengurt, E.** Neurotensin Induces Protein Kinase C-Dependent Protein Kinase D Activation and DNA Synthesis in Human Pancreatic Carcinoma Cell Line PANC-1. *Cancer Res.* 62:1632-40, 2002.
22. Waldron RT, **Rozengurt E.** Protein kinase C phosphorylates protein kinase D activation loop Ser744 and Ser748 and releases autoinhibition by the pleckstrin homology domain. *J. Biol. Chem.* 278:154-63, 2003.
23. Yuan J, Slice LW, Gu J, **Rozengurt E.** Cooperation of Gq, Gi, and G12/13 in Protein Kinase D Activation and Phosphorylation Induced by Lysophosphatidic Acid. *J. Biol. Chem.* 278: 4882-4891, 2003.
24. Guha, S, Lunn, JA, Santiskulvong C, **Rozengurt E.** Neurotensin Stimulates Protein Kinase C-dependent Mitogenic Signaling in Human Pancreatic Carcinoma Cell Line PANC-1. *Cancer Res.* 63:2379-2387, 2003.
25. Chiu T, Santiskulvong C, and **Rozengurt E.** ANG II stimulates PKC-dependent ERK activation, DNA synthesis, and cell division in intestinal epithelial cells. *Am. J. Physiol. Gastrointest. Liver Physiol.* 285: G1-11, 2003.

26. Hunger-Glaser I, Salazar EP, Sinnett-Smith J, and **Rozengurt E**. Bombesin, lysophosphatidic acid, and epidermal growth factor rapidly stimulate focal adhesion kinase phosphorylation at Ser-910: requirement for ERK activation. *J. Biol. Chem.* 278: 22631-43, 2003.
27. Rey O, Yuan J, Young SH, and **Rozengurt E**. Protein kinase C $\alpha$ /protein kinase D3 nuclear localization, catalytic activation, and intracellular redistribution in response to G protein-coupled receptor agonists. *J. Biol. Chem.* 278: 23773-85, 2003
28. Waldron, R. T., Rey, O., Zhukova, E., and **Rozengurt, E**. Oxidative stress induces protein kinase C-mediated activation loop phosphorylation and nuclear redistribution of protein kinase D. *J Biol Chem*, 279: 27482-27493, 2004.
29. Sinnett-Smith J, Zhukova E, Hsieh N, Jiang X, **Rozengurt E**. Protein kinase D potentiates DNA synthesis induced by Gq-coupled receptors by increasing the duration of ERK signaling in Swiss 3T3 cells. *J. Biol. Chem.* 279:16883-16893, 2004.
30. Rey, O., Reeve, Jr., J.R., Zhukova, E., Sinnett-Smith, J., **Rozengurt, E**. G protein-coupled receptor-mediated phosphorylation of the activation loop of protein kinase D: dependence on plasma membrane translocation and protein kinase C $\epsilon$ . *J. Biol. Chem.* 279: 34361-34372, 2004.
31. Lunn, J.A., **Rozengurt, E**. Hyperosmotic stress induces rapid FAK phosphorylation at tyrosines 297 and 577: Role of Src-family kinases and Rho-family GTPases. *J. Biol. Chem.* 279:45266-45278, 2004
32. Chiu, T., Santiskulvong, C., and **Rozengurt, E**. EGF receptor transactivation mediates ANG II-stimulated mitogenesis in intestinal epithelial cells through the PI3-kinase/Akt/mTOR/p70S6K1 signaling pathway. *Am. J. Physiol. Gastrointest. Liver Physiol.*, 288: G182-194, 2005.
33. Rey, O., Young, S.H., Yuan, J., Slice, L., **Rozengurt, E**. Amino acid-stimulated Ca<sup>2+</sup> oscillations produced by the Ca<sup>2+</sup>-sensing receptor are mediated by a phospholipase C/Inositol 1,4,5-Trisphosphate-independent pathway that requires G12, Rho, filamin-A and the actin cytoskeleton. *J Biol Chem.* 280:22875-2282, 2005.
34. Fan R.S., Jacamo R.O., Jiang X., Sinnett-Smith J., **Rozengurt, E**. G protein-coupled receptor activation rapidly stimulates focal adhesion kinase phosphorylation at Ser-843. Mediation by Ca<sup>2+</sup>, calmodulin, and Ca<sup>2+</sup>/calmodulin-dependent kinase II. *J Biol Chem.* 280:24212-20, 2005.
35. **Rozengurt, E**, Rey, O., and Waldron, R. T. Protein Kinase D Signaling. *J Biol Chem*, 280: 13205-13208, 2005.
36. Guha S, Eibl G, Kisfalvi K, Fan RS, Burdick M, Reber H, Hines OJ, Strieter R, **Rozengurt E**: Broad-spectrum G protein-coupled receptor antagonist, [D-Arg1,D-Trp5,7,9,Leu11]SP: a dual inhibitor of growth and angiogenesis in pancreatic cancer. *Cancer Res.* 65: 2738-2745, 2005.
37. Rey, O., Young, S. H., Papazyan, R., Shapiro, M. S., and **Rozengurt, E**. Requirement of the TRPC1 Cation Channel in the Generation of Transient Ca<sup>2+</sup> Oscillations by the Calcium-sensing Receptor. *J. Biol. Chem.*, 281: 38730-38737, 2006.
38. Yuan, J., Rey, O., and **Rozengurt, E**. Activation of protein kinase D3 by signaling through Rac and the alpha subunits of the heterotrimeric G proteins G12 and G13. *Cell Signal*, 18: 1051-1062, 2006.
39. Rey, O., Papazyan, R., Waldron, R. T., Young, S. H., Lippincott-Schwartz, J., Jacamo, R., and **Rozengurt, E**. The nuclear import of protein kinase D3 requires its catalytic activity. *J Biol Chem*, 281: 5149-5157, 2006.
40. Jiang, X., Jacamo, R., Zhukova, E., Sinnett-Smith, J., and **Rozengurt, E**. RNA interference reveals a differential role of FAK and Pyk2 in cell migration, leading edge formation and increase in focal adhesions induced by LPA in intestinal epithelial cells. *J Cell Physiol*, 207: 816-828, 2006.
41. Chen MC, Wu SV, Reeve JR, Jr., **Rozengurt E**: Bitter stimuli induce Ca<sup>2+</sup> signaling and CCK release in enteroendocrine STC-1 cells: role of L-type voltage-sensitive Ca<sup>2+</sup> channels. *Am J Physiol Cell Physiol* 291: C726-739, 2006.
42. Rozengurt N, Wu SV, Chen MC, Huang C, Sternini C, **Rozengurt E**: Colocalization of the {alpha}-subunit of gustducin with PYY and GLP-1 in L cells of human colon. *Am J Physiol Gastrointest Liver Physiol.* 291:G792-802, 2006.
43. Young SH, **Rozengurt E**: Quinacrydine conjugates conjugated to bombesin or ANG II label the cognate G protein-coupled receptor in living cells. *Am J Physiol Cell Physiol.* 290: C728-732, 2006.
44. Chiu, T., Leung, W. Y., Moyer, M. P., Strieter, R. M., and **Rozengurt, E**. Protein Kinase D2 mediates lysophosphatidic acid-induced interleukin-8 production in nontransformed, human colonic epithelial cells through NF- $\kappa$ B. *Am J Physiol Cell Physiol*, 292:C767-77, 2007.
45. Lunn JA, Jacamo R, **Rozengurt E**. Preferential phosphorylation of focal adhesion kinase (FAK) tyrosine-861 is critical for mediating an anti-apoptotic response to hyperosmotic stress. *J Biol Chem.* 282:10370-9, 2007.

46. Jacamo, R., Jiang, X., Lunn, J. A., and **Rozengurt, E.** FAK phosphorylation at Ser-843 inhibits Tyr-397 phosphorylation, cell spreading and migration. *J Cell Physiol*, 210: 436-444, 2007.
47. Kisfalvi K, Rey O, Young SH, Sinnett-Smith J, **Rozengurt E.** Insulin potentiates Ca<sup>2+</sup> signaling and phosphatidylinositol 4,5 -bisphosphate hydrolysis induced by Gq protein-coupled receptor agonists through an mTOR-dependent pathway. *Endocrinology*. 148:3246-57, 2007
48. Santiskulvong C, **Rozengurt E.** Protein kinase C $\alpha$  mediates feedback inhibition of EGF receptor transactivation induced by Gq-coupled receptor agonists. *Cell Signal* 19: 1348-1357, 2007.
49. **Rozengurt E.** Mitogenic signaling pathways induced by G protein-coupled receptors. *J Cell Physiol*. 213, 589 – 602, 2007.
50. Yuan J, **Rozengurt E.** PKD, PKD2, and p38 MAPK mediate Hsp27 serine-82 phosphorylation induced by neurotensin in pancreatic cancer PANC-1 cells. *J Cell Biochem*. 103, 648-662, 2008
51. Jacamo R, Sinnett-Smith J, Rey O, Waldron RT, **Rozengurt E.** Sequential protein kinase C (PKC)-dependent and PKC-independent protein kinase D catalytic activation via Gq-coupled receptors: differential regulation of activation loop Ser-744 and Ser-748 phosphorylation. *J Biol Chem*. 283: 12877-12887, 2008.
52. Yuan J, Lugea A, Zheng L, Gukovsky I, Edderkaoui M, **Rozengurt E**, Pandolfi SJ: Protein kinase D1 mediates NF- $\kappa$ B activation induced by cholecystokinin and cholinergic signaling in pancreatic acinar cells. *Am J Physiol Gastrointest Liver Physiol*. 2008; [Epub ahead of print].

### C. Research Support.

#### Ongoing research support

R01 DK56930 Rozengurt (PI) 06/01/06-5/31/11  
NIH/NIDDK

##### *GI Peptide Signaling Through Tyrosine Phosphorylation*

The major goals of this project are to identify the intracellular mechanisms leading to rapid GI peptide-induced tyrosine phosphorylation of focal adhesion proteins in Swiss 3T3 cells and the intestinal epithelial cell line IEC-6, a well established model of restitution. They are also to determine the role of EGFR transactivation in signaling GI peptide-mediated mitogenesis.

Role: PI

R01 DK55003 Rozengurt (PI) 07/01/08-06/30/12  
NIH NIDDK

##### *Gastrointestinal Peptide Signaling through PKC/PKD*

The major goals of this project are to characterize the activation of the PKC/PKD pathway and define the role of PKD in GI peptide signal transduction.

Role: PI

P30 DK 41301 Rozengurt (PI) 12/01/04 – 11/30/09  
NIH/NIDDK

##### *CURE: Digestive Diseases Research Core Center*

The CURE: Digestive Diseases Research Core Center is composed of a cohesive group of physicians and basic scientists with strong independent peer-reviewed grant-supported research programs in the biology of the gut, with special emphasis upon regulation of mucosal cell function, gut neuroscience and signal transduction mechanisms.

Role: PI

#### Completed Research Support

1 P50 CA 090388-01 Dubinett (PI) 06/01/01-12/31/07

National Cancer Institute

UCLA Lung Cancer SPORE, section on "Neuropeptide Signaling Antagonist for SCLC Therapy"

A major objective of this grant proposal is to develop antagonists of neuropeptide action that have broader spectrum than specific receptor antagonists and to elucidate their mechanism of action.

Role: Section Principal Investigator.