Begoña Díaz, Ph.D.

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Education

Ph.D. Biology	Madrid Autonoma University (Madrid, Spain). Incidence and regulation of programmed cell death during early neurogenesis in the embryo retina.	1999
M.S. Cell Biology	Madrid Complutense University (Madrid, Spain). Effect of glucocorticoids on fetal rat liver development.	1994
B.S. Biology	Madrid Complutense University (Madrid, Spain)	1992

Research Interests

- Hypoxia, Notch and EGFR signaling in cancer invasion and resistance to therapy
- Redox signaling and cancer cell invasiveness
- Regulation of invadopodia formation and activity

Rese

search Experience	
• Research Assistant Professor. Cancer Center, Sanford-Burnham Medical Research Institute, San Diego, California. Novel functions of PDK1 in the nucleus of cancer cells.	2013-
• Staff Scientist. Cancer Center, Sanford-Burnham Medical Research Institute, San Diego, California. Supervisor: Dr. Sara A. Courtneidge. Novel isoforms of Tks5 in mammalian development. Regulation of cancer invasiveness by hypoxia through Notch and ADAM12-dependent shedding of EGFR ligands. NADPH oxidase-dependent redox signaling and cancer invasiveness.	2007-2013
• Staff Scientist. Molecular Oncology Program. Spanish National Cancer Center, Madrid (Spain). Supervisor: Dr. Eduardo Moreno. <i>Cell competition between germline stem cells in Drosophila</i> .	2005-2007
• Associate Specialist, Step II. Molecular and Cell Biology Department, University of California at Berkeley, Berkeley, California. Supervisor: Dr. G. Steven Martin. RhoA activity in Src-mediated transformation.	2003-2004
• Post-doctoral Scholar. Molecular and Cell Biology Department, University of California at Berkeley, Berkeley, California. Supervisor: Dr. G. Steven Martin. Oncogenic Src in E2F-1 phosphorylation and activity.	1999-2003
• Ph.D. Candidate. Spanish National Research Council and Madrid Autonoma University, Madrid (Spain). Regulation of neuroblast survival by pro-insulin during early retinal neurogenesis.	1995-1999
• Masters Thesis Candidate. Cell Biology Department. Complutense University of Madrid, Madrid (Spain). Effects of glucocorticoids in the structure of the rat fetal liver.	1994-1992

• Undergraduate Research Assistant. Cell Biology Department. Complutense

1990-1992
University of Madrid, Madrid (Spain). Perfusion and isolation of proteins from rat liver.

Publications (peer-reviewed)

- P. Cejudo-Martin, A. Yuen, N. Vlahovich, P. Lock, S.A. Courtneidge and <u>B. Díaz.</u> Genetic disruption of the Sh3pxd2a gene reveals and essential role in mouse development and the existence of a novel isoform of Tks5. *PLoS ONE* 9 (9): e107674.

 http://www.ncbi.nlm.nih.gov/pubmed/25259869
- K.L. Burger, B.S. Learman, A.K. Boucherle, S.J. Sirintrapun, S. Isom, <u>B. Díaz</u>, S.A.
 Courtneidge and D.F. Seals. Src-dependent Tks5 phosphorylation regulates invadopodia-associated invasion in prostate cancer cells. *The Prostate* Feb; 74(2): 134-48.
 http://www.ncbi.nlm.nih.gov/pubmed/24174371
- <u>B. Díaz</u>*, A. Yuen, S. Iizuka, S. Higashiyama and S.A. Courtneidge. Notch increases the shedding of HB-EGF by ADAM12 to potentiate invadopodia formation in hypoxia. *Journal of Cell Biology* 201 (2), 279-292. (*) <u>Corresponding Author</u>

 http://www.ncbi.nlm.nih.gov/pubmed/23589494
- J. M. Munson, L. Fried, S.A. Rowson, M.Y. Bonner, L. Karumbaiah, <u>B. Díaz</u>, S.A. 2012 Courtneidge, U. Knaus, DJ. Brat, JL. Arbiser, RV. Bellamkonda. Anti-invasive adjuvant therapy with Imipramine Blue enhances chemotherapeutic efficacy against glioma. *Science Translational Medicine* 4,127ra36. http://www.ncbi.nlm.nih.gov/pubmed/22461640
- <u>B. Díaz</u> and S.A. Courtneidge. Redox signaling at invasive microdomains in cancer cells. *Free Radical Biology and Medicine* Jan 15; 52(2): 247-56. http://www.ncbi.nlm.nih.gov/pubmed/22033009
- DA Murphy, <u>B. Díaz</u>, PA. Bromann, JH Tsai, Y Kawakami, J Maurer, RA Stewart, JC
 Izpisúa-Belmonte and SA Courtneidge (2011). A Src-Tks5 pathway is required for neural crest migration during embryonic development. *PLoS ONE* 6(7): e22499.

 http://www.ncbi.nlm.nih.gov/pubmed/21799874
- B. Díaz, G. Shani, I. Pass, D. Anderson, M. Quintavalle and S.A. Courtneidge. Tks5-dependent, Nox-mediated generation of reactive oxygen species is necessary for invadopodia formation. *Science Signaling* Sep 15; 2(88): ra53. http://www.ncbi.nlm.nih.gov/pubmed/19755709
- D. Gianni, <u>B. Díaz</u>, N. Taulet, B. Fowler, S.A Courtneidge and GM Bokoch. Novel p47^{phox}related organizers regulate NADPH oxidase 1 (Nox1) activity and localization. *Science*Signaling Sep 15; 2(88): ra54. http://www.ncbi.nlm.nih.gov/pubmed/19755710
- C. Rhiner*, <u>B. Díaz</u>*, M. Portela, JF. Poyatos, I. Fernández-Ruiz, JM. López-Gay, O. Gerlitz and E. Moreno. Persistent competition among stem cells and their daughters in the Drosophila ovary germline niche. *Development* 136, 995-1006. (*) <u>Equal contribution</u> http://www.ncbi.nlm.nih.gov/pubmed/19211674

• B. Blouw, D.F. Seals, I. Pass, B. Díaz, and S.A. Courtneidge. A role for the 2008 podosome/invadopodia scaffold protein Tks5 in tumor growth in vivo. European Journal of Cell Biology 87, 555-567. http://www.ncbi.nlm.nih.gov/pubmed/18417249 • D.E. Shvartsman, J.C. Donaldson, B. Díaz, O. Gutman, G.S. Martin, and Y.I. Henis. Src 2007 kinase activity and SH2 domain regulate the dynamics of Src association with lipid and protein targets. Journal of Cell Biology 178 (4), 675-86. http://www.ncbi.nlm.nih.gov/pubmed/17698610 • B. Díaz and Moreno E. The competitive nature of cells. Experimental Cell Research 306, 317-2005 322. http://www.ncbi.nlm.nih.gov/pubmed/15925586 • R.L. Berdeaux*, B. Díaz*, L.C. Kim, and G.S. Martin. Active Rho is localized to podosomes 2004 induced by oncogenic Src and is required for their assembly and function. Journal of Cell Biology 166 (3), 317-323. (*) Equal contribution. http://www.ncbi.nlm.nih.gov/pubmed/15289494 · B.L. Webb, B. Díaz, G.S. Martin and F. Lai. A reporter system for reverse transfection cell 2003 arrays. Journal of Biomolecular Screening 8, 620-624. http://www.ncbi.nlm.nih.gov/pubmed/14711387 · C. Machín, C. Rua C., B. Díaz and RM Arahuetes. Effects of endogenous and exogenous 2001 glucocorticoids on liver differentiation. Acta Biologica Hungarica 52, 63-74 http://www.ncbi.nlm.nih.gov/pubmed/11396842 • B. Díaz, J. Serna, F. de Pablo and E.J. de la Rosa. In vivo regulation of cell death by 2000 embryonic (pro) insulin and the insulin receptor during early retinal neurogenesis. Development 127,1641-1649. http://www.ncbi.nlm.nih.gov/pubmed/10725240 • B. Díaz, B. Pimentel, F. de Pablo and E.J. de la Rosa. Apoptotic cell death of proliferating 1999 neuroepithelial cells in the embryonic retina is prevented by insulin. European Journal of Neuroscience 11, 624-1632. http://www.ncbi.nlm.nih.gov/pubmed/10215915 • A.V. Morales, M. Hadjiargyrou, B. Díaz, C. Hernandez-Sanchez, F. de Pablo and E.J. de la 1998 Rosa. Heat shock proteins in retinal neurogenesis: identification of the PM1 antigen as the chick Hsc70 and its expression in comparison to that of other chaperones. European Journal of Neuroscience 10, 3237-3245. http://www.ncbi.nlm.nih.gov/pubmed/9786217 • E.J. de la Rosa, B. Díaz and F. de Pablo. Organoculture of the chick embryonic neuroretina. 1998 Cellular and Molecular Procedures in Developmental Biology. Current Topics in Developmental Biology Volume 36, 133-144. Academic Press. http://www.ncbi.nlm.nih.gov/pubmed/9342525 • F. de Pablo, C. Alarcon, B. Díaz, M. Garcia-de Lacoba, A. Lopez-Carranza, A.V. Morales, B. 1996 Pimentel, J. Serna and E.J. de la Rosa. Complementary roles of the insulin family of factors and receptors in early development and neurogenesis. International Journal of Developmental Biology. Supplement 1, 109-110. http://www.ncbi.nlm.nih.gov/pubmed/9087719

· C. Machín, J. Sierra, B. Díaz, and Rua C. Ultrastructural variations of the rat fetal adrenal 1995 cortex after maternal bilateral adrenalectomy and exogenous glucocorticoid administration. Acta Biologica Hungarica 46 (87-98), http://www.ncbi.nlm.nih.gov/pubmed/8714766 Additional peer-reviewed publications/Editorial Highlights • A. Yuen and B. Díaz. The impact of hypoxia in pancreatic cancer invasion and metastasis. 2014 Hypoxia July 2014. Vol 2014: 2; 91-106. http://dx.doi.org/10.2147/HP.S52636 • B. Diaz. Invadopodia detection and gelatin degradation assay. Bio-protocol. Vol 3, Iss 24. 2013 Dec. 20. http://www.bio-protocol.org/e997 • B. Short. Hypoxia takes invadopodia up a Notch. Journal of Cell Biology 201 (2):168. 2013 Highlight of B. Diaz et al. (Journal of Cell Biology, 2013). http://jcb.rupress.org/content/201/2/168.3.full · Faculty of 1000 Prime. Article Recommendation for B. Diaz et al. (Journal of Cell Biology, 2013 2013). http://f1000.com/prime/718018380?subscriptioncode=ad612d69-bcd2-489b-83f6-2a37d9dfa9c3 • K. Legg. Two-leg trip to invasion. Cell Migration Gateway. Featured Article of May: 2013 B.Diaz et al. (Journal of Cell Biology, 2013). http://www.cellmigration.org/cmg_update/2013/130501/full/cmg178.shtml • Block and Gorin. Aiding and abetting roles of NOX oxidases incellular transformation. 2012 Nature Reviews in Cancer. Highlights and recommends B.Diaz and Courtneidge (Free Radical Biology and Medicine 2012). http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3711509/ · A.M. Weaver. Regulation of cancer invasion by reactive oxygen species and Tks family 2009 scaffold proteins. Science Signaling Sep15; 2(88): pe56. Highlight of B. Diaz et al. and Gianni et al. (Science Signaling 2009). http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2893140/ • W.A. Wells. Rho in podosomes. Journal of Cell Biology 166 (3): 305. Highlight of R. 2004 Berdeaux, B. Diaz et al. (Journal of Cell Biology, 2004). http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2253780/

Invited talks

- Mechanisms and Models of Cancer Symposium. The Salk Institute, La Jolla (California). Aug 2013
 Notch increases the shedding of HB-EGF by ADAM12 to potentiate invadopodia formation in hypoxia.
- Annual Cancer Center Retreat. Sanford-Burnham Medical Research Institute. La Jolla
 (California). Notch increases the shedding of HB-EGF by ADAM12 to potentiate invadopodia
 formation in hypoxia.

• Gordon Research Conference in Matrix Metalloproteinases. Barga (Italy). Notch increases the shedding of HB-EGF by ADAM12 to potentiate invadopodia formation in hypoxia.	May 2013
 Cold Spring Harbor Laboratory Meeting on Phosphorylation, Signaling, and Disease. Cold Spring Harbor, (New York). Reactive Oxygen Species are necessary for invadopodia formation. 	May 2009
• VII National Congress of the Spanish Society of Cell Biology. Córdoba (Spain). Regulation of proliferation and cell death during retinal neurogenesis.	Sept 1997
Editorial Positions and Contributions	
• Editorial Board Member, Mutations & Cancer Studies.	2013-
• Editorial Board Member, Applied Scientific Reports	2013-
• Invited Reviewer for Journal of Cell Biology, Molecular Human Reproduction, Oncogene, Cell Adhesion & Migration, Bio-Protocol, Onco-Targets and Therapy	2013-
• Reviewer of over 20 manuscripts for high-impact journals.	2007-
Affiliations/Memberships	
• Invadosome Consortium. Regular Member.	2013-
• American Association for Cancer Research (AACR). Regular Member.	2009-
• Spanish Society of Biochemistry and Molecular Biology. Regular Member.	1999-
Honors and Awards	
• Top Abstract Presentation Award. Second Annual Sanford-Burnham Institute Cancer Center Retreat.	2013
• Pre-doctoral Fellowship from the Researcher Training Program of the Madrid Region. Competitive International Award.	1995-1999
Teaching Experience	
• Teaching Assistant, Madrid Autonoma University. Graduate course on Stem Cells. Lecture on: Competition between stem cells in Drosophila.	2005
 Teaching Assistant, Madrid Complutense University. Graduate course on Animal Histology. Laboratory courses. 	1993-1994

Laboratory training experience (Students)

- Bernardo Lara, Intern Student. UCSD Minority Undergraduate Student Program.
 Currently a Graduate student at UCSD. Small compounds in invadopodia formation in human cells (tissue culture, immunofluorescence and microscopy, IC50 calculation).
- Christopher Abdullah. Graduate Student, Biomedical Sciences Program. UCSD, San
 Diego, California. Contact time: 12 weeks. Currently Ph.D. candidate at UCSD, San
 Diego. Optimization of HIF-1a depletion in human cells (tissue culture, siRNA
 transfection, immunofluorescence and immunoblotting).
- Marshall Peterman. Graduate Student, Biomedical Sciences Program. UCSD, San Diego,
 California. Contact time: 12 weeks. Currently a Ph.D. candidate at UCSD, San Diego.
 Cdk5, Src, MAPK and PI3K inhibitors in invadopodia formation (tissue culture, IC50 calculation, immunofluorescence, immunoblotting)
- Cora Bergantiños. Graduate Student. Molecular Biology Department. Madrid Autonoma
 University. Spain. Contact time: 16 weeks. Currently a Post-Doctoral Researcher at
 Columbia University (New York). Generation of a new Drosophila line (Drosophila crosses, dissection and staining of imaginal discs).
- Andrea Tu. Molecular and Cellular Department at UC Berkeley. Contact time: 6 weeks.
 She obtained her Ph.D. and is currently Applications Manager at ProteinSimple (San Francisco). Isolation of Rhotekin-GST fusion protein for Rho activity assays (bacteria transformation, bacteria culture, recombinant protein purification).
- Daniel Ballon. Molecular and Cellular Department at UC Berkeley. Contact time: 12 weeks. He obtained her Ph.D. and is currently Principal Consultant at California Legislature (Sacramento). Analysis of E2F-1 phosphorylation by Src (tissue culture, transfection, immunoprecipitation, immunoblotting)

Laboratory supervision and training experience (Laboratory and Research Assistants)

- Jonathan Lo, undergraduate student from UCSD. Laboratory Assistant at Sanford

 Burnham Medical Research Institute. Labware cleaning, autoclaving, preparation of
 laboratory solutions and tail digestion for mouse genotyping.
- Angela Yuen, B.S. from UCSD. Research Assistant I at Sanford Burnham Medical
 Research Institute. Currently a Pharmacy Intern at University Medical Center of
 Southern Nevada. High-throughput screening for Nox inhibitors (tissue culture,
 transfection, assay optimization); Stability and phosphorylation of a novel isoform of ths5
 (immunoprecipitation, immunoblotting, molecular cloning). Co-authored three
 manuscripts under my supervision.
- Lomi Kim. M.S. from Ohio State University. Research Assistant at UC Berkeley. She is currently Project Manager at OmniVision Technologies (San Francisco). Analysis of E2F-1 tyrosine phosphorylation (tissue culture, immunoprecipitation, immunoblotting,

molecular cloning and site-directed mutagenesis). Co-authored one manuscript under my supervision.

Vanessa Tse, undergraduate student from UCSD. Laboratoty Assistant at Sanford
 Burnham Medical Research Institute. She is currently B.S. from UCSD and Lead

 Veterinary Technician at Irvine Great Park Animal Hospital (Irvine). Labware cleaning, autoclaving, preparation of laboratory solutions and plates for bacterial growth.

Maria Fernanda Camargo. M.S. from Mexico National Autonoma University. Laboratory
 Assistant at Sanford Burnham Medical Research Institute. She is currently Staff
 Research Associate III at UCSD. Analysis of Tks5 mRNA expression in breast cancer cell
 lines (cDNA synthesis by retrotranscription, tissue culture, molecular cloning).

• Waisen Tong, undergraduate student from UCSD. Laboratory Assistant at Sanford
Burnham Medical Research Institute. He is currently a Pharmacy Student at Thomas
Jefferson University. Labware cleaning, autoclaving, preparation of laboratory solutions and plates for bacterial growth.

Meetings and Courses

• Mechanisms and Models of Cancer Symposium. The Salk Institute for Biological Studies, La Jolla (California)	Aug 2013
• Gordon Research Conference in Matrix Metalloproteinases. Italy.	May 2013
• Mechanisms and Models of Cancer Symposium. The Salk Institute for Biological Studies, La Jolla (California).	Aug 2011
• Molecular Therapeutics of Cancer Research Conference. Asilomar, (California).	July 2010
 Protein Phosphorylation and Cell Signaling Meeting. The Salk Institute for Biological Studies. La Jolla, California. 	Aug 2010
• San Diego Lab Management Course. The Salk Institute for Biological Studies. La Jolla, California.	Feb 2008
• Tyrosine phosphorylation and Cell signaling Meeting. The Salk Institute for Biological Studies. La Jolla, California.	Aug 2002
• Programmed Cell Death Regulation: Basis Mechanisms and Therapeutic Opportunities. Incline Village, Nevada.	Mar 2000
• VI Symposium in Oncogenes. Ramón Areces Foundation. Madrid (Spain)	Oct 1998
• VII National Congress of the Spanish Society for Cell Biology. Cordoba (Spain).	Sep 1997
• International Course on Advances in Molecular Bases of Neurobiology. Ramón Areces Foundation. Madrid (Spain)	May 1996
• Madrid Complutense University, Summer Courses Series: Brain Development. El Escorial, Madrid (Spain).	Aug 1995
• X International Course for Post-graduates in Perinatal Biochemistry. Madrid	Mar 1994

Autonoma University and Ramón Areces Foundation. Madrid (Spain).

Abstract/Poster Presentations

Córdoba (Spain).

• <u>B. Díaz</u> , A. Yuen, S. Iizuka, S. Higashiyama and SA. Courtneidge. <i>Notch increases the shedding of HB-EGF by ADAM12 to potentiate invadopodia formation in hypoxia</i> . Mechanisms and Models of Cancer Symposium. The Salk Institute for Biological Studies, La Jolla.	Aug 2013
• <u>B. Díaz</u> , A. Yuen, S. Iizuka, S. Higashiyama and SA. Courtneidge. <i>Notch increases the shedding of HB-EGF by ADAM12 to potentiate invadopodia formation in hypoxia</i> . Gordon Research Conference in Matrix Metalloproteinases. Barga (Italy).	May 2013
• R.L. Berdeaux, <u>B. Díaz</u> L.C. Kim, and G.S. Martin. <i>Active Rho is localized to Src-induced podosomes and is required for their assembly and function.</i> Protein Phosphorylation and Cell Signaling Meeting. The Salk Institute for Biological Studies. La Jolla.	Jun 2004
• E.J. de la Rosa, <u>B. Díaz</u> , E. Rubio, B. Pimentel and Flora de Pablo. <i>Distribution and regulation of cell death occurring in early neural development</i> . II Meeting of the Spanish Society of Developmental Biology. Barcelona (Spain).	Jun 1999
• <u>B. Díaz</u> , B. Pimentel, E.J. de la Rosa and F. de Pablo. <i>Apoptosis in proliferating neuroepithelial cells during neurogenesis</i> . Workshop on Cellular Regulatory Mechanisms: Choices, Time and Space Institute Juan March de Estudios e Investigaciones. Madrid (Spain).	May 1998
• E.J. de la Rosa, <u>B. Díaz</u> , B. Pimentel and Flora de Pablo. <i>Are apoptosis and proliferation balanced by insulin in retinal neurogenesis?</i> Meeting on Programmed Cell Death Cold Spring Harbor Laboratory. Cold Spring Harbor (New York)	Sep 1997
• B. Pimentel, <u>B. Díaz</u> , F. de Pablo and E.J. de la Rosa. <i>Proliferation-Differentiation-Apoptosis: a balance that drives neurogenesis</i> . 13 th Lecture Course on Biophysics and Molecular Biology. Molecular Mechanisms of Embryonic Development University of Trieste and Udine. Udine (Italy).	Jul 1997
• F. de Pablo, B. Pimentel, <u>B. Díaz</u> and E.J. de la Rosa. <i>Insulin and IGF in early development and retinal neurogenesis</i> . European Society for Comparative Physiology and Biochemistry. Barcelona (Spain).	Sep 1997
• F. de Pablo, M. García de Lacoba, B. Díaz , C. Alarcón and E.J. de la Rosa. <i>The insulin/IGFs system in retinal neurogenesis</i> . Workshop on Signal Transduction in Neuronal Development and Recognition. Instituto Juan March de Estudios e Investigaciones. Madrid (Spain)	Apr 1997
• <u>B.Díaz</u> , F. de Pablo and E.J. de la Rosa. Regulation of proliferation and cell death during retinal neurogenesis. VII National Congress of the Spanish Society of Cell Biology.	Sep 1997