

BIOGRAPHICAL SKETCH

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NAME Adriana Heguy	POSITION TITLE		
eRA COMMONS USER NAME	Associate Lab Member, Human Oncology and Pathogenesis Program		
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Universidad de la Republica, Montevideo, Uruguay	B.Sc.	1982	Biology
University of Southern California, Los Angeles, CA	PhD	1986	Microbiology

A. Positions and Honors

1985 -1988 Post-doctoral fellow, Rockefeller University, Dept. of Biochemistry, New York, NY
 1988 -1992 Senior Staff Scientist, Sclavo Research Center, Sienna, Italy
 1992 -1993 Senior Scientist, OSI Pharmaceuticals, Inc., Uniondale, NY
 1993 -1996 Program Manager, Proprietary R&D and MMD collaboration, OSI Pharmaceuticals, Inc, Uniondale, NY
 1996 -1997 Associate Director, Virology, Pharmaceuticals, Inc., Uniondale, NY
 1997 -1999 Director, Virology, Pharmaceuticals, Inc., Uniondale, NY
 2000 - 2001 Assistant Professor, Albert Einstein College of Medicine and Senior Research Associate, North Shore-LIJ Health System, Manhasset, NY
 2001 - 2007 Assistant Professor, Department of Genetic Medicine, Weill Medical College of Cornell University, New York, NY
 2007 – Present Associate Lab Member, Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York, NY

Honors and Awards

1986-1988: Damon Runyon-Walter Winchell Cancer Research Fund Post-doctoral Fellowship, Rockefeller University, New York, New York.
 1985-1986: Charles Heidelberger Memorial Predoctoral Award in Cancer Research, University of Southern California, Los Angeles, California.
 1983-1984: Charles Heidelberger Memorial Predoctoral fellowship in Cancer Research, University of Southern California, Los Angeles, California.

B. Selected Peer-reviewed Publications

Richards, R.I, Heguy, A, and Karin, M. Structural and functional analysis of the human metallothionein-IA gene: differential induction by metal ions and glucocorticoids. *Cell* 37, 263-272 (1984).
 Scholer, A., Haslinger, A., Heguy, A., Holtgreve H. and Karin, M. In vivo competition between metallothionein regulatory elements and the SV40 enhancer. *Science*, 32, 76-80 (1986).
 Karin, M., Haslinger, A., Heguy, A., Dietlin T. and Cooke T. Metal responsive elements act as positive regulators of human metallothionein IIA enhancer activity. *Mol. Cell. Biol.* 7, 606-613 (1987).
 Scheidereit, C., Heguy, A., and Roeder R.G. Identification and purification of human lymphoid specific octamer binding protein (OTF-2) that activates transcription an immunoglobulin promoter in vitro. *Cell*, 51, 783-793 (1988).
 Sherman, P.A., Basta, P.V., Heguy, A., Wloch, M.K., Roeder R.G. and Ting J.P.-Y. The octamer element is a B-Lymphocyte-specific regulatory element of the HLA-DRA gene promoter. *Proc. Natl. Acad. Sci. USA* 86, 6739-6743 (1989).

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- Pierani, A., Heguy, A., Fujii, H. and Roeder, R.G. Activation of octamer-containing promoters by either octamer-binding transcription 1 (OTF-1) or OTF-2 and requirement of an additional B-cell-specific component for optimal transcription of immunoglobulin promoters. *Mol. Cell. Biol.* 10, 6204-6215 (1990).
- Heguy, A., Baldari, C., Bush, K., Nagele, R., Newton, R.C., Robb, R.J., Horuk, R., Telford, J.L. and Melli, M. Internalization and nuclear localization of IL-1 are not sufficient for function. *Cell Growth and Diff.* 2, 311-315 (1991).
- Baldari, C.T., Macchia, G., Heguy, A., Melli, M. and Telford, J.L. Cyclosporin A blocks calcium-dependent pathways of gene activation. *J. Biol. Chem.* 266, 19103-19108 (1991).
- Heguy, A., Baldari, C.T., Macchia, G., Telford, J.L. and Melli, M. Amino acids conserved in interleukin-1 receptors and the Drosophila Toll protein are essential in IL-1R signal transduction. *J. Biol. Chem.* 267, 2605-2609 (1992).
- Guida, A., Heguy, A., and Melli, M. The chicken IL-1 receptor. Differential evolution of the cytoplasmic and extracellular domains. *Gene* 111, 239-243 (1992).
- Heguy, A., Baldari, C.T., Ghiara, P and Telford, J.L. A type II/type I interleukin 1 chimeric receptor transduces a type I receptor signal in T cells. *J. Biol. Chem.* 268:10490-10494 (1993).
- Baldari, C.T., Heguy, A. and Telford, J.L. Calcium-dependent cyclosporin A-sensitive activation of the Interleukin-2 promoter by p56^{lck}. *J. Biol. Chem.* 268: 8406-8409 (1993).
- Baldari, C.T., Heguy, A. and Telford, J.L. Ras protein activity is essential for T-cell antigen receptor signal transduction. *J. Biol. Chem.* 268, 2693-2698 (1993).
- Baldari, C. T., Heguy, A. and Telford, J.L. Calcium dependent activation of the NF-AT transcription factor by p59fyn. *FEBS Lett.* 323:233-235 (1993).
- Baldari, C.T., Heguy, A., DiSomma, M. M. and Telford, J.L. Inhibition of T-cell antigen receptor signalling by overexpression of p120GAP. *Cell Growth and Diff.* 5:95-8 (1994).
- Heguy, A., Stewart, A. A., Haley, J. D., Smith, D. E. and Foulkes, J. G. Gene expression as a target for new drug discovery. *Gene Expr.* 4:337-344 (1995).
- Heguy, A., Cai, P., Meyn, P., Houck, D., Russo, S., Michitsch, R., Pearce, C., Katz, B., Bringmann, G., Feineis, D., Taylor, DL and Tyms, AS. Isolation and characterization of the fungal metabolite 3-O-methylviridicatin as an inhibitor of tumor necrosis factor alpha-induced human immunodeficiency virus replication. *Antiviral Chemistry and Chemotherapy* 9:149-155 (1998).
- Kaplan R, Luettich K, Heguy A, Hackett NR, Harvey B-G, Crystal RG. Monoallelic upregulation of the imprinted H19 gene in airway epithelium of phenotypically normal cigarette smokers. *Cancer Res.* 2003; 63: 1475-1482
- Hackett NR, Heguy A, Harvey B-G, Luettich K, Kaplan R, Crystal RG. Variability of antioxidant-related gene expression in the airway epithelium of cigarette smokers. *Am J Respir Cell Mol Bio* 2003; 29: 331-343
- Heguy A, Harvey B-G, O'Connor TP, Hackett NR, Crystal RG. Sampling dependent upregulation of gene expression in sequential samples of human airway epithelial cells. *Mol Med* 2003; 9: 200-208.
- De B, Heguy A, Leopold PL, Wasif N, Korst RJ, Hackett NR, Crystal RG. Intrapleural administration of a serotype 5 adeno-associated virus coding for α 1-antitrypsin mediates persistent, high lung and serum levels of α 1-antitrypsin. *Mol Ther* 2004; 10:1003-1010
- Worgall S, Heguy A, Kuettich K, O'Connor TP, Harvey B-G, Quadri LEN, Crystal RG. Similarity of patterns in gene expression of human alveolar macrophages evoked by *Pseudomonas aeruginosa* and *Burkholderia cepacia*. *Infec Immun* 2005; 73:5262-5268
- Heguy A, Crystal RG. Intrapleural 'outside-in' gene therapy: therapeutics for organs of the chest via gene transfer to the pleura. *Curr Opin Mol Ther.* 2005 7:440-53.
- De BP, Heguy A, Hackett NR, Ferris B, Leopold PL, Lee J, Pierre L, Gao G, Wilson JM, Crystal RG. High levels of persistent expression of alpha1-Antitrypsin mediated by the nonhuman primate serotype rh.10 adeno-associated virus despite preexisting immunity to common human adeno-associated viruses. *Mol Ther.* 2006 13(1):67-76.
- Heguy A, O'Connor TP, Luettich K, Worgall S, Ciecuch AA, Harvey B-G, Hackett NR, Crystal RG. Gene expression profiling of human alveolar macrophages of phenotypically normal smokers and non-smokers reveals a previously unrecognized subset of genes modulated by cigarette smoking. *J Mol Med* 2006; 84:318-328.

Publications (continued)

- Carolan BJ, Heguy A, Harvey BG, Leopold PL, Ferris B and Crystal RG. Upregulation of expression of the ubiquitin carboxyl terminal hydrolase L1 gene in human airway epithelium of cigarette smokers. *Cancer Res.* 2006; 66:10729-40.
- Heguy A*, Harvey B-G*, Leopold PL, Carolan B, Ferris B, Crystal RG. Modification of gene expression of the small airway epithelium in response to cigarette smoking. *J. Mol. Med.* 2007; 85(1):39-53. *Authors Heguy and Harvey contributed equally to this study
- Gelbman, BD, Heguy A, O'Connor TP, Zabner, J, Crystal RG. Upregulation of pirin expression by chronic cigarette smoking is associated with bronchial epithelial cell apoptosis. *Resp.Res.* 2007; 8;8:10.
- Heguy, A., Harvey B-G, Leopold PL, Dolgalev, I, Raman, T, Crystal RG. Responses of the human airway epithelium transcriptome to *in vivo* injury. *Physiol. Genomics* 2007; 29(2):139-48.
- Tilley AE, Harvey BG, Heguy A, Hackett NR, Wang R, O'Connor TP, Crystal RG. Downregulation of the Notch Pathway in Human Airway Epithelium in Association with Smoking and COPD. *Am J Respir Crit Care Med.* 2009;179(6):457-66.
- Kilpivaara O, Mukherjee S, Schram AM, Wadleigh M, Mullally A, Ebert BL, Bass A, Marubayashi S, Heguy A, Garcia-Manero G, Kantarjian H, Offit K, Stone RM, Gilliland DG, Klein RJ and Levine RL. A germline JAK2 SNP is associated with predisposition to the development of JAK2 V617F-positive myeloproliferative neoplasms. *Nature Genetics* 2009;41(4):455-9
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