

## CURRICULUM VITAE

### René Daniel, M.D., Ph.D.

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U.S. status: permanent resident

**SUMMARY: Internal Medicine physician (Resident, PGY-3, TJU) and established scientist (part time Associate Professor and Principal Investigator, NIH funded) at the Division of Infectious Diseases, TJU, fields of HIV, DNA repair, gene therapy, and aging**

### EDUCATION:

1<sup>st</sup> Medical School, Charles University, Prague, Czech Rep. Degree: **M.D.** 1991 (June)  
SUNY, HSC at Brooklyn, NY Graduate Prog. Microbiology  
September 1991- May 1993 (transferred to Temple in May 1993)  
Fels Institute for Cancer Res. & Mol. Biol., Temple U. Degree: **Ph.D.** Mol. Biol. & Genetics  
May 1993- November 1996  
(Ph.D. thesis defense November 1996, diploma issued January 1997)

### POSTGRADUATE TRAINING:

#### Research:

Postdoctoral Fellow, Dr. P.M.C. Wong's Laboratory, Fels Institute for Cancer Research, Temple University, Philadelphia, PA, cancer research November 1996 - August 1997  
Postdoctoral Associate, Fox Chase Cancer Center, Institute for Cancer Research, Philadelphia, PA HIV research September 1997- September 2003

#### Clinical:

Residency, Internal Medicine Program 2012-2015 (expected graduation date 2015)

### JOB EXPERIENCE:

Assistant Professor, Department of Medicine, Thomas Jefferson University, Philadelphia, PA, HIV research  
September 2003-December 2008  
Associate Professor, Department of Medicine, Thomas Jefferson University, Philadelphia, PA, HIV/gene therapy research 2008-2012  
Associate Professor, Department of Medicine, Thomas Jefferson University, Philadelphia, PA, HIV/gene therapy research 2013-present

### AWARDS AND HONORS:

ASH Meeting 1996 - Travel Award 1996  
Fox Chase Cancer Center Board of Associates Fellowship 1999  
Tobacco Formula Grant Investigator (Principal Investigator, \$414,000, 1/1/03-12/31/03) 2002  
Howard Temin **K01** Award (Principal Investigator, 7/1/03-6/30/08) 2003  
Sigma Xi 2005  
AAAS Science – STKE Editor's choice (Issue 283, May 10 2005, Daniel and Pomerantz,

Nat Cell Biol. 7, 452-453, 2005)	2005
W.W. Smith Charitable Trust AIDS Research Award (Principal Investigator)	2006
Certificate of Appreciation (Kimmel Cancer Center, for outstanding service)	2006
Vice-President, Sigma Xi Jefferson Chapter	2006
Cellular co-factors in retroviral transduction, <b>R01</b> (Principal Investigator, 4/1/07-1/31/12)	2007
W.W. Smith Charitable Trust AIDS Research Award (Principal Investigator)	2007
President, Sigma Xi Jefferson Chapter	2007-2008
<b>R21</b> (Principal Investigator, 2008-2010)	
Organizing Committee, Centennial Retrovirus Meeting, Prague	2010
<b>R21</b> (Principal Investigator, 11/1/13-present)	2013
<b>National Academy of Inventors</b> , member	2013

## RECENT PATENTS AND INVENTIONS

U.S. Patent 7.736,848 (Cellular targets for treatment of retroviral infection)	2010
Invention disclosure/provisional patent application No.61/146,137 (Targeting of integration of retroviral vectors by manipulating integration cofactors)	2009/10
Invention disclosure "A quick PCR-based method to measure the frequency of integration within or in the vicinity of active genes"	2008

## MEMBERSHIP IN PROFESSIONAL SOCIETIES:

American Society for Microbiology	2004-2012
Sigma Xi	2005-2012
International AIDS Society	2005-2012
ACP	2012-present

## SERVICE TO PROFESSIONAL PUBLICATIONS AND ORGANIZATIONS:

**Ad hoc reviewer:** Gene, Leukemia Research, Journal of Infectious Diseases, Nature Reviews Immunology. Future Virology, Medical Science Monitor, Journal of Pathology, Royal Society of Chemistry, Journal of Neuroimmune Pharmacology, Mechanisms of Ageing and Development

**Editorial board:** Open Virology Journal since 2007  
International Journal of Virology since 2006

**Ad hoc reviewer:** Israeli Science Foundation since 2009  
**(grants)** TAG study section since 2009  
ZRG1 GGG-N(99)S ARRA Special Emphasis Panel 2009  
German Research Foundation since 2009  
ANR (France) since 2010

## PUBLICATIONS AND PRESENTATIONS:

### ORAL PRESENTATIONS AT INTERNATIONAL MEETINGS:

Daniel, R., Wong, P.M.C., and Chung, S.-W. Involvement of cdc2 and p53 in c-abl-mediated apoptosis. The Annual Meeting of the American Society of Hematology. Blood 88 (10S): 449, 1996.

Daniel, R., Katz, R.A., and Skalka, A.M. Involvement of DNA-PK in retroviral integration. Molecular mechanisms in DNA replication and recombination 1999. Keystone symposia on molecular and cellular biology.

Daniel, R., Katz, R.A., and Skalka, A.M. Involvement of DNA-PK in retroviral integration. 1999 Cold Spring Harbor Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.

Daniel, R., Katz, R.A., Merkel, G., Hittle, J.C., Yen, T.J., and Skalka, A.M. A compensatory pathway of retroviral DNA integration mediated by ATM kinase. 2000 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.

Daniel, R., Katz, R.A., and Skalka, A.M. Retroviral infection induces complexes of NHEJ proteins with retroviral integrase. 2001 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.

Smith, J.A., Wang, F.-X., and Daniel, R. Nijmegen breakage syndrome protein 1 controls the ATM-dependent DNA damage response to HIV-1 integration. Keystone Symposia on Molecular and cellular determinants of HIV Pathogenesis, 2006.

Smith JA, Ndoye, A.M.N., Geary, K., Lisanti, M.P. , Igoucheva, O., Daniel, R. HIV-1 integration site preferences in pluripotent stem cells, CRM 2010.

### **PEER-REVIEWED PUBLICATIONS:**

1. Kren, V., Pravenec, M., Bila, V., Daniel, R., Stursa, P., Hnevkovsky, P. and Kurtz, T.W. Genetic analysis of polydactyly-luxate syndrome in the rat. *Transplant. Proc.* 22: 2588-2589, 1990.
2. Daniel, R., Cai, Y., Wong, P.M.C. and Chung, S.-W. Deregulation of c-abl-mediated cell growth after retroviral transfer and expression of antisense sequences. *Oncogene 10*: 1607-1614, 1995.
3. Daniel, R., Wong, P.M.C. and Chung, S.-W. Isoform-specific functions of c-abl: Type 1 is necessary for differentiation and Type IV is inhibitory to apoptosis. *Cell Growth Diff.* 7: 1141-1148, 1996.
4. Daniel, R., Chung, S.-W., Chen, H. and Wong, P.M.C. Retroviral gene transfer of antisense sequences results in reduction of c-abl and induction of apoptosis in hemopoietic cells. *J. Biomed. Sci.* 5: 383-394, 1998.
5. Le, Q., Daniel, R., Chung, S.-W., Kang, A.D., Eisenstein, T.K., Sultzer, B.M., Simpkins, H. and Wong, P.M.C. Involvement of c-abl tyrosine kinase in lipopolysaccharide-induced macrophage activation. *J. Immunol.* 160: 3330-3336, 1998.
6. Daniel, R., Katz, R.A. and Skalka, A.M. A role for DNA-PK in retroviral DNA integration. *Science* 284: 644-647, 1999.
7. Daniel, R., Katz, R.A., Merkel, G., Hittle, J.C., Yen, T.J. and Skalka, A.M. Wortmannin potentiates integrase-mediated killing of lymphocytes and reduces the efficiency of stable transduction by retroviruses. *Mol. Cell. Biol.* 21: 1164-1172, 2001.
8. Daniel, R., Litwin, S., Katz, R.A. and Skalka, A.M. Computational analysis of retrovirus-induced *scid* cell death, *J. Virol.* 75: 3121-3128, 2001.
9. Daniel, R., Chung, S.-W., Eisenstein, T.K., Sultzer, B.M., and Wong, P.M. Specific association of Type I c-Abl with Ran GTPase in lipopolysaccharide-mediated differentiation. *Oncogene 20*: 2618-25, 2001.
10. Taganov, K., Daniel, R., Katz, R.A., Favorova, O., and Skalka, A.M. Characterization of retroviral-host DNA junctions in NHEJ-deficient cells, *J Virol.* 75: 9549-52, 2001.
11. Daniel, R.\*, Kao, G., Taganov, K., Favorova, O., Merkel, G., Yen, T.J., Katz, R.A., and Skalka, A.M. Evidence that the retroviral DNA integration process triggers an ATR-dependent DNA damage response, *Proc. Natl. Acad. Sci. USA* 100:4778-4783,2003.

12. Cortellino, S., Turner, D., Masciullo, V., Schepis, F., Albino, D., Daniel, R., Skalka, A.M., Meropol, N.J., Alberti, C., Larue, L., and Bellacosa A. The base excision repair enzyme MED1 mediates DNA damage response to antitumor drugs and is associated with mismatch repair system integrity. *Proc Natl Acad Sci USA* 100:15071-15076, 2003.
13. Daniel, R., Myers, C.B., Taganov, K., Greger, J.G., Merkel, G., Weber, I.T., Torshin, I., Harrison, R.W., and Skalka, A.M. Characterization of a novel inhibitor of retroviral integrases, *AIDS Res Hum Retroviruses*. 20:135-44, 2004.
14. Taganov, K., Cuesta, I., Daniel, R., Cirillo, L.A., Katz, R.A., Zaret, K.S., and Skalka, A.M. Integrase-specific enhancement and suppression of retroviral DNA integration by compacted chromatin structure in vitro. *J Virol*. 78:5848-55, 2004.
15. Daniel, R., Greger, J.G., Katz, R.A., Taganov, K.D., Wu, X., Kappes, J.C., and Skalka, A.M. Evidence that stable retroviral transduction and cell survival following DNA integration depend on components of the nonhomologous end joining repair pathway. *J Virol*. 78:8573-81, 2004.
16. Daniel, R., Ramcharan, J., Rogakou, E., Taganov, K.D., Greger J.G., Bonner, W., Nussenzweig, A., Katz, R.A., and Skalka, A.M. Histone H2AX is phosphorylated at sites of retroviral DNA integration but is dispensable for postintegration repair. *J Biol Chem*. 279:45810-4, 2004.
17. Daniel, R.\*, Marusich, E., Argyris, E., Zhao, R.Y., Skalka, A.M., and Pomerantz, R.J. Caffeine inhibits human immunodeficiency virus type 1 transduction of nondividing cells. *J. Virol*. 79:2058-65, 2005.
18. Nunnari, G., Argyris, E., Fang, J., Mehlman, K., Pomerantz, R.J., and Daniel, R.\*. Inhibition of HIV-1 replication by the ATR and ATM inhibitor caffeine and caffeine-related methylxanthines. *Virology*, 335: 177-184, 2005.
19. Nunnari, G., Xu, Y., Acheampong, E.A., Fang, J., Daniel, R., Zhang, C., Mukhtar, M., and Pomerantz, R.J. Exogenous IL-7 induces Fas-mediated human neuronal apoptosis: potential effects during human immunodeficiency virus type 1 infection. *J. Neurovirol*. 11: 319-28, 2005.
20. Smith, J.A., and Daniel, R.\*. Following the path of the virus: the exploitation of host DNA repair mechanisms by retroviruses. Review. *ACS Chemical Biology* 1: 217-226, 2006.
21. Daniel, R.\* DNA repair in HIV-1 infection: A case for inhibitors of cellular co-factors? Review. *Current HIV Research* 4: 411-21, 2006.
22. Smith, J.A., Nunnari, G., Preuss, M., Pomerantz, R.J., and Daniel, R.\*. Pentoxifylline suppresses transduction by HIV-1-based vectors. *Intervirology* 50:377-386, 2007.
23. Pabla, N., Huang, S., Mi, Q.-S., Daniel, R., and Dong, Z. ATR-Chk2 signaling in p53 activation and DNA damage response during cisplatin-induced apoptosis. *J Biol Chem* 283: 6572-6583, 2008.
24. Smith, J.A., Wang, F.-X., Zhang, H., Wu, K.-J., Williams, K.J. and Daniel, R.\*. Evidence that the Nijmegen breakage protein, an early sensor of double-strand DNA breaks (DSB), is involved in HIV-1 post-integration repair by recruiting the ataxia telangiectasia mutated kinase in a process similar to, but distinct from, cellular DSB repair. *Virology J* 5: 11, 2008.
25. Huang, H., Fletcher, L., Beeharry, N., Daniel, R., Yen, T.Y., and Muschel, R.J. Abnormal cytokinesis after X irradiation in tumor cells that override the G2 DNA damage checkpoint. *Cancer Res* 68: 3724-32, 2008.

26. Daniel, R.\*, and Smith, J.A. Integration site selection by retroviral vectors: molecular mechanism and clinical consequences. Review. *Human Gene Therapy* 19: 558-67, 2008.
27. Silvers, R., Smith, J.A., Schowalter, M., Litwin, S., Liang, Z., Geary, K., and Daniel, R.\* Modification of Integration Site Preferences of an HIV-1-based Vector by expression of a novel synthetic protein. *Hum Gene Ther* 21: 337-49, 2010.
28. Smith J.A., Ndoeye, A.M.N., Geary, K., Lisanti, M.P., Igoucheva O., Daniel, R.\* A role for the Werner syndrome protein in the epigenetic inactivation of the pluripotency factor Oct4. ***Aging Cell*** 9: 580-91, 2010.
29. Smith J.A., Yeung, J., Kao, G.D., Daniel, R.\*. A role for the histone deacetylase HDAC4 in the life-cycle of HIV-1-based vectors. *Virol J* 7: 237, 2010.
30. Smith J.A., Daniel, R.\*. Up-regulation of HIV-1 transduction in nondividing cells by double-strand DNA break-inducing agents. *Biotechnol Lett.* 33: 243-52, 2011.
31. Markman J.L., Silvers, R.M., Ndoeye, A.M.N., Geary, K., Alvarado, D., Smith, J.A., Daniel, R.\*. HIV-1 integration site preferences in pluripotent cells. *Frontiers Biosc (elite ed.)* 3:453-62, 2011.
32. Liang, Z., Diamond, M., Smith, J.A., Schnell, M., Daniel, R.\*. Proliferating cell nuclear antigen is required for loading of the SMCX/KMD5C histone demethylase onto chromatin. *Epigenetics Chromatin* 13: 18, 2011.
33. Smith, J.A., Daniel, R.\*. Stem cells and Aging: a chicken-or-the-egg issue? *Aging Dis* 3: 260-8, 2012.
34. Papayannakos, C., Daniel, R.\*. Understanding lentiviral vector chromatin targeting: working to reduce insertional mutagenic potential for gene therapy. *Gene Ther* Nov 22 2012. Epub ahead of print.
35. Vakil S., Daniel, R., and Short W. Newly diagnosed AIDS with multiple opportunistic infections despite a recent negative HIV test. *The Medicine Forum* 14: 7-9, 2013.

\* Corresponding Author

#### **REVIEWS, NEWS&VIEWS ARTICLES AND BOOK CHAPTERS:**

1. Chung, S.-W., Daniel, R., Wong, B.Y. and Wong, P.M.C. The ABL genes in normal and abnormal cell development. *Crit. Rev. Oncog.* 7: 33-48, 1996.
2. Daniel, R.\* and Pomerantz, R.J. ATM: HIV-1's Achilles Heel? ***Nat. Cell Biol.***, 7:452-453, 2005.
3. Daniel, R.\* and Pomerantz, R.J. Double-strand break DNA repair in retroviral infections. *Research Advances in Virology* 3:1-19, 2005.
4. Smith, J.A., and Daniel, R.\*. Following the path of the virus: the exploitation of host DNA repair mechanisms by retroviruses. *ACS Chemical Biology* 1: 217-226, 2006.
5. Daniel, R.\* DNA repair in HIV-1 infection: A case for inhibitors of cellular co-factors? *Current HIV Research* 4: 411-21, 2006.
6. Nunnari, G., Smith, J.A., and Daniel, R.\* HIV-1 Tat and AIDS-associated cancer: targeting the cellular anti-cancer barrier? *J Exp Clin Canc Res* 27:3, 2008.

7. Daniel, R.\*, and Smith, J.A. Intricacies of integration. In Genetic Recombination Research Progress, Nova Science Publishers (NY), 2008.
8. Daniel, R.\*, and Smith, J.A. Integration site selection by retroviral vectors: molecular mechanism and clinical consequences. Review. Human Gene Therapy: 558-67, 2008.
9. Smith, J.A., and Daniel, R.\* Caffeine and HIV-1 infection. In Caffeine and Human Health, Nova Science Publishers (NY), 2009.
10. Smith J.A., Daniel, R.\*. Stem cells and Aging: a chicken-or-the-egg issue? Aging Dis 3: 260-8, 2012.
11. Papayannakos C., Daniel R.\*. Understanding lentiviral vector chromatin targeting: working to reduce insertional mutagenic potential for gene therapy. Gene Ther Nov 22 2012. Epub ahead of print.

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#### **ABSTRACTS:**

1. Daniel, R., Wong, P.M.C., and Chung, S.-W. Retroviral transfer of antisense sequences results in effective inhibition of transformation mediated by an activated oncogene. The Annual Meeting of the American Society of Hematology. Blood 82 (10S): 120, 1993.
2. Daniel, R., Chung, S.-W., and Wong, P.M.C. Isoform-specific functions of c-abl: Type I is necessary for differentiation and type IV is inhibitory to apoptosis. Twelve Annual Meeting on Oncogenes 1996.
3. Daniel, R., Wong, P.M.C., and Chung, S.-W. Involvement of cdc2 and p53 in c-abl-mediated apoptosis. The Annual Meeting of the American Society of Hematology. Blood 88 (10S): 449, 1996.
4. Daniel, R., Katz, R.A., and Skalka, A.M. Involvement of DNA-PK in retroviral integration. Molecular mechanisms in DNA replication and recombination 1999. Keystone symposia on molecular and cellular biology.
5. Daniel, R., Katz, R.A., and Skalka, A.M. Involvement of DNA-PK in retroviral integration. 1999 Cold Spring Harbor Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
6. Daniel, R., Katz, R.A., Merkel, G., Hittle, J.C., Yen, T.J., and Skalka, A.M. A compensatory pathway of retroviral DNA integration mediated by ATM kinase. 2000 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
7. Daniel, R., Katz, R.A., Taganov, K., Wu, X., Kappes, J.C., and Skalka, A.M. DNA-PK is required for efficient stable transduction by HIV-1-based vectors. 2001 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
8. Daniel, R., Katz, R.A., and Skalka, A.M. Retroviral infection induces complexes of NHEJ proteins with retroviral integrase. 2001 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
9. Litwin, S., Daniel, R., Katz, R.A. and Skalka, A.M. Computational analysis of retrovirus-induced *scid* cell death. 2001 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
10. Taganov, K., Daniel, R., Katz, R.A., Favorova, O., and Skalka, A.M. Characterization of retroviral-host DNA junctions in NHEJ-deficient cells. 2001 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
11. Daniel, R., Kao, G., Taganov, K., Favorova, O., Merkel, G., Yen, T.J., Katz, R.A., and Skalka, A.M.

- Retroviral DNA integration requires DNA damage sensing by ATR. 2002 Meeting on Cell Biology of DNA. Cold Spring Harbor Laboratory, NY.
12. Nunnari, G., Argyris, E., Fang, J., Mehlman, K.E., Pomerantz, R.J., and Daniel, R. Inhibition of HIV-1 replication by caffeine and caffeine-related methylxanthines. 2005 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
  13. Daniel, R., Greger, J.G., Katz, R.A., Taganov, K.D., Wu, X., Kappes, J.C., Pomerantz, R.J., and Skalka, A.M. Role of the non homologous end-joining pathway in post-integration repair. 2005 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
  14. Nunnari, G., Argyris, E., Fang, J., Mehlman, K.E., Pomerantz, R.J., and Daniel, R. Inhibition of HIV-1 replication by caffeine and caffeine-related methylxanthines. Keystone Symposia on Molecular and cellular determinants of HIV-1 Pathogenesis, 2005.
  15. Nunnari, G., Argyris, E., Fang, J., Mehlman, K.E., Pomerantz, R.J., and Daniel, R. Inhibition of HIV-1 replication by caffeine and caffeine-related methylxanthines. IAS Conference on HIV-1 Pathogenesis and Treatment, 2005.
  16. Nunnari, G., Carter, A.M., Smith, J.A., Skalka, A.M., Pomerantz, R.J., and Daniel, R. Molecular Analysis of Pentoxifylline-Mediated Suppression of HIV-1 Replication. 2006 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
  17. Smith, J.A., Wang, F.-X., and Daniel, R. Nijmegen breakage syndrome protein 1 controls the ATM-dependent DNA damage response to HIV-1 integration. Keystone Symposia on Molecular and cellular determinants of HIV Pathogenesis, 2006.
  18. Smith, J.A., Wang, F.-X., and Daniel, R. Nijmegen breakage syndrome protein 1 controls the ATM-dependent DNA damage response to HIV-1 integration. 2006 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
  19. Smith, J.A. and Daniel, R. Up-regulation of HIV-1 transduction in nondividing cells by double-strand DNA break-inducing agents. Keystone Symposia on Molecular and cellular determinants of HIV-1 Pathogenesis, 2007.
  20. Smith, J.A. and Daniel, R. Up-regulation of HIV-1 transduction in nondividing cells by double-strand DNA break-inducing agents. 2007 Meeting on Retroviruses. Cold Spring Harbor Laboratory, NY.
  21. Smith, JA, Kao, G., Greger, J.G., Skalka, A.M., and Daniel, R. A role for histone deacetylase HDAC4 in HIV-1 transduction. Keystone symposia on HIV-1 Immunobiology, 2009.
  22. Smith JA, Ndoeye, A.M.N., Geary, K., Lisanti, M.P. , Igoucheva, O., Daniel, R. HIV-1 integration site preferences in pluripotent stem cells, CRM 2010.