
NAME: WENRUI DUAN

CURRENT ADDRESS:

6715 Stillhouse LN,
Dublin, OH 43016

E-mail: wduan@fiu.edu

CITIZENSHIP: USA

ACADEMIC EXPERIENCE:

October 2016 –
Associate Professor, Faculty of Herbert Wertheim College of Medicine
Department of Human & Molecular Genetics, the Florida International University, Miami, Florida.

January 2010- October 2016
Assistant Professor- Research, Faculty of Medical School
Division of Medical Oncology, Department of Internal Medicine and Comprehensive Cancer Center, The Ohio State University, Columbus, Ohio.

July 2004 – December 2009
Research Scientist, **Principal Investigator**, Comprehensive Cancer Center, The Ohio State University, Columbus, Ohio.

September 1999 – June 2004
Post-doc/research associate, Ohio State University Medical Center, The Ohio State University, Columbus, Ohio.

September 1992 – August 1999
Graduate Research /Teaching Associate, College of Biological Science, The Ohio State University, Columbus, Ohio.

December 1987 - June 1991
Lecturer: Department of Biology, Inner Mongolia Normal University. Huhhot, China.

1982 – 1987
Teaching Associate: Department of Biology, Inner Mongolia Normal University. Huhhot, China.

EDUCATION:

Ph. D. Molecular Genetics, December, 1999
Department of Molecular Genetics, the Ohio State University, Columbus, OH

M. S. Zoology, December, 1994
College of Biological Science, the Ohio State University, Columbus, OH

M. S. Biology, July 1989
Inner Mongolia Normal University, Huhhot, China

B. S. Biology, 1982
Inner Mongolia University, Huhhot, China

PUBLICATIONS:

Original Reports

1. Kalvala A, Gao L, Aguila B, Dotts K, Rahman M, Nana-Sinkam P, Zhou X, Wang QE, Amann J, Otterson GA, Villalona-Calero MA, **Duan W*** Rad51C-ATXN7 fusion gene expression in colorectal tumors. *Mol Cancer*. 15(1):47. In press 2016,
PMID: 27296891

2. Villalona-Calero MA, **Duan W**, Zhao W, Shilo K, Schaaf LJ, Thurmond J, Westman JA, Marshall J, Xiaobai L, Ji J, Rose J, Lustberg M, Bekaii-Saab T, Chen A, Timmers C. Veliparib Alone or in Combination with Mitomycin C in Patients with Solid Tumors With Functional Deficiency in Homologous Recombination Repair. *J Natl Cancer Inst*. 108(7). In press, 2016 Jul.
PMID: 26848151

3. Cui T, Srivastava AK, Han C, Yang L, Zhao R, Zou N, Qu M, **Duan W**, Zhang X, Wang QE. XPC inhibits NSCLC cell proliferation and migration by enhancing E-Cadherin expression. *Oncotarget*. 6(12):10060-72. 2015.
PMID: 25871391

4. Kalvala A, Gao L, Aguila B, Reese T, Otterson GA, Villalona-Calero MA, **Duan W*.** Overexpression of Rad51C splice variants in colorectal tumors. *Oncotarget.* 6(11):8777-87. 2015.
PMID: 25669972

5. **Duan W***, Gao L, Aguila B, Kalvala A, Otterson GA, Villalona-Calero MA. Fanconi anemia repair pathway dysfunction, a potential therapeutic target in lung cancer. *Front Oncol.* 4:368. doi: 10.3389/fonc.2014.00368. 2014.
PMID: 25566506
PMCID: PMC4271581

6. Ding H, Casto B, Deng Y, Grill K, **Duan W**, Zhang N, Cole S, Perle K, Pan X, Kinghorn DA, D'Ambrosioet SM. Avocado Extract Inhibits 7, 12-Dimethylbenz[a]anthracene (DMBA)-Induced Carcinogenesis in Hamster Cheek Pouches. *Med Chem S1*: 008. doi:10.4172/2161-0444.S1-008, 2014

7. Singh M, Leasure JM, Chronowski C, Geier B, Bondra K, **Duan W**, Hensley LA, Villalona-Calero M, Li N, Vergis AM, Kurmasheva RT, Shen C, Woods G, Sebastian N,

Fabian D, Kaplon R, Hammond S, Houghton P, Palanichamy K, Chakravarti A. FANCD2 is a Potential Therapeutic Target and Biomarker in Alveolar Rhabdomyosarcoma Harboring the PAX3/FOXO1 Fusion Gene. *Clin Cancer Res*. 20(14):3884-95. 2014.
PMID: 24787670

8. Eisfeld AK, Schwind S, Hoag KW, Walker CJ, Liyanarachchi S, Patel R, Huang X, Markowitz J, **Duan W**, Otterson GA, Carson WE 3rd, Marcucci G, Bloomfield CD, de la Chapelle A. NRAS isoforms differentially affect downstream pathways, cell growth, and cell transformation. *Proc Natl Acad Sci U S A.* 111(11):4179-84, 2014.
PMID:24586049,
PMCID: PMC3964043

9. Shilo K, Wu X, Sharma S, Welliver M, **Duan W**, Villalona-Calero M, Fukuoka J, Sif S, Baiocchi R, Hitchcock CL, Zhao W, Otterson GA. Cellular localization of protein arginine methyltransferase-5 correlates with grade of lung tumors. *Diagn Pathol.* 8(1):201, 2013.
PMID:24326178.
PMCID:PMC3933389

10. **Duan W***, Gao L, Zhao W, Leon M, Sadee W, Webb A, Resnick K, Wu X, Ramaswamy B, Cohn DE, Shapiro C, Andreassen PR, Otterson GA, Villalona-Calero MA. Assessment of FANCD2 nuclear foci formation in paraffin embedded tumors; a potential patient enrichment strategy for treatment with DNA interstrand crosslinking agents. *Transl Res*. 161(3):156-64, 2013.
PMID:23063585
PMCID:PMC3755957

11. Wu Y, **Duan W**, Otterson GA, Lee LJ, Nana-Sinkam SP. Research Highlight: miRNA and platinum-based chemotherapy response in non-small-cell lung cancer. *Personalized Medicine*, 9 (3):329-332, 2012.

12. Yin DT, Wang Q, Chen L, Liu MY, Han C, Yan Q, Shen R, He G, **Duan W**, Li JJ, Wani A, Gao JX. Germline stem cell gene PIWIL2 mediates DNA repair through relaxation of chromatin. *PLoS One*. 6(11):e27154, 2011.
PMID: 22110608
PMCID: PMC3217960

13. **Duan W***, Gao L, Wu X, Wang L, Nana-Sinkam P, Otterson GA, Villalona-Calero MA. MicroRNA-34a is an important component of PRIMA-1 induced apoptotic network in human lung cancer cells. *Int J Cancer*. 127(2): 313–20, 2010.
PMID: 19921694

14. Yan F, Wu X, Crawford M, **Duan W**, Wilding EE, Gao L, Nana-Sinkam SP, Villalona-Calero MA, Baiocchi RA, Otterson GA. The search for an optimal DNA, RNA, and protein detection by in situ hybridization, immunohistochemistry, and solution-based methods. *Methods.* 52(4):281-6, 2010.
PMID: 20888418

PMCID: PMC3375896

15. **Duan W***, Gao L, Wu X, Hade EM, GaoJX, Ding H, Barsky SH, Otterson GA, Villalona-Calero MA. Expression of a mutant p53 results in an age-related demographic shift in spontaneous lung tumor formation in transgenic mice. *PLoS One*. 4(5):e5563, 2009.
PMID: 19440353
PMCID: PMC2680060

16. Xu Y, Kolesar JM, Schaaf LJ, Drengler R, **Duan W**, Otterson G, Shapiro C, Kuhn J, Villalona-Calero MA. Phase I and pharmacokinetic study of mitomycin C and celecoxib as potential modulators of tumor resistance to irinotecan in patients with solid malignancies. *Cancer Chemother Pharmacol*. 63(6):1073-82, 2009
PMID: 18795290

17. Ding H, Han C, Guo D, Wang D, **Duan W**, Chen CS, D'Ambrosio SM. Sensitivity to the non-COX inhibiting celecoxib derivative, OSU03012, is p21(WAF1/CIP1) dependent. *Int J Cancer*. 123(12):2931-8, 2008.
PMID: 18798266
PMCID: PMC2605165

18. **Duan W**, Gao L, Jin D, Otterson GA, Villalona-Calero MA. Lung specific expression of a human mutant p53 affects cell proliferation in transgenic mice. *Transgenic Research* 17(3): 355-66, 2008.
PMID: 17968669

19. Chen L, Shen R, Ye Y, Pu XA, Liu X, **Duan W**, Wen J, Zimmerer J, Wang Y, Liu Y, Lasky LC, Heerema NA, Perrotti D, Ozato K, Kuramochi-Miyagawa S, Nakano T, Yates AJ, Carson Iii WE, Lin H, Barsky SH, Gao JX. Precancerous Stem Cells Have the Potential for both Benign and Malignant Differentiation. *PLoS ONE*. 14;2(3):e293, 2007.
PMID: 17356702

20. **Duan W**, Villalona-Calero MA**.** MDM2 (transformed mouse 3T3 cell double minute 2, p53 binding protein) (12q15). *Atlas Genet Cytogenet Oncol Haematol.* 11 (2):158-164, 2007.

21. Villalona-Calero M, Schaaf L, Phillips G, Otterson G, Panico K, **Duan W**, Kleiber B, Shah M, Young D, Wu WH, Kuhn J. Thalidomide and celecoxib as potential modulators of irinotecan's activity in cancer patients. *Cancer Chemother Pharmacol*. 59(1):23-33, 2007.

22. **Duan W**, Gao L, Wu X, Zhang Y, Otterson GA, Villalona-Calero MA. Differential response between the p53 ubiquitin protein ligases Pirh2 and MdM2 following DNA Damage. *Exp Cell Res* 312(17):3370-8, 2006.

23. **Duan W,** Villalona-Calero MA . RCHY1 (ring finger and CHY zinc finger domain containing 1). *Atlas Genet Cytogenet Oncol Haematol*. 10(3):385-390, 2006.

24. **Duan W**, Gao L, Druhan LJ, Zhu WG, Morrison C, Otterson GA, Villalona-Calero MA. Expression of Pirh2, a newly identified ubiquitin protein ligase, in lung cancer. *J Natl Cancer Inst*. 96(22):1718-21, 2004.

25. Zhu WG, Hileman T, Ke Y, Wang P, Lu S, **Duan W**, Dai Z, Tong T, Villalona-Calero MA, Plass C, Otterson GA. 5-Aza-2'-deoxycytidine Activates the p53/p21Waf1/Cip1 Pathway to Inhibit Cell Proliferation. *J Biol Chem*. 279(15):15161-6, 2004

26. Ding H, **Duan W**, Zhu WG, Srinivasan K, Otterson GA, Villalona-Calero MA. p21 response to DNA damage induced by genistein and etoposide in human lung cancer cells. *Biochem Biophys Res Commun (BBRC)*. 305(4):950-6, 2003.

27. Zhu WG, Srinivasan K, Dai Z, **Duan W**, Ding H, Yee L, Villalona-Calero MA, Plass C, Otterson G. Hypermethylation induced decrease in Sp1/Sp3 binding is associated with reduced $p21^{Cip1}$ expression in response to depsipeptide treatment. *Molecular and Cellular Biology (MCB)***.** 23(12):4056-65, 2003.

28. **Duan W**, Ding H, Subler MA, Zhu WG, Zhang H, Stoner GD, Windle JJ, Otterson GA, Villalona-Calero MA. Lung-specific expression of human mutant p53-273H is associated with a high frequency of lung adenocarcinoma in transgenic mice. *Oncogene*. 21(51):7831-8, 2002.

29. **Duan W**, Ding H, Zhu WG, Srinivasan K, Otterson GA, Villalona-Calero MA. RT-PCR heteroduplex analysis permits differentiation of transgene and host gene expression in a transgenic animal model. *Biotechniques*. 33(1):58-66, 2002.

30. Zhu WG, Dai Z, Ding H, Srinivasan K, Hall J, **Duan W**, Villalona-Calero MA, Plass C, Otterson GA. Increased expression of unmethylated CDKN2D by 5-aza-2'-deoxycytidine in human lung cancer cells. *Oncogene*. 20(53):7787-96, 2001.

31. **Duan W.** and Fuerst PA. Isolation of a sex linked DNA sequence in cranes**.** *J. Heredity*, 92:392-7, 2001.

32. Huyvaert KP, Anderson DJ, Jones TC, **Duan W**, Parker PG. Extra-pair paternity in waved albatrosses. *Mol Ecol*. 9(9):1415-9, 2000.

33. Booton CG, Kaufman L, Chandler M, **Duan W,** Fuerst PA. Evolution of the ribosomal RNA internal transcribed spacer one (ITS1) in Cichlid of the Lake Victoria region. *Mol. Phy. Evol*., 11(2): 273-82, 1999.

Note: * corresponding author

Abstracts (Peer Reviewed, Published).

1. **Duan W**, Ding H, Subler M, Windle J, Otterson G, Villalona-Calero M. Lung specific expression of mutant p53 (273H) in mice. *Proceedings of the American Association for Cancer Research* (42) 2001, P 221 (abstr 1185)

2. Ding H, **Duan W**, Zhu W, Ju R, Subler M, Otterson G, Villalona-Calero, M. Mechanisms of regulation of CHK2 expression after exposure to the topoisomerase II inhibitor genistein. *Proceeding of AACR-NCI-RORTC International Conference*. 2001, P 139 (abstr 708).

3. Kolesar J, Miller J, **Duan W**. Drengler R, Felton S, Schaaf L, Von Hoff D, Kuhn J, Villalona-Calero M. TI Induction in PBMC Predicts Response to MMC/CPT-11. *Proceedings of American Society of Clinical Oncology* 2002, P115a (abstr 456)

4. Zhu W, Dai Z, Srinivasam K, Ding H, **Duan W**, Villalona M, Plass C, Otterson G. Methylated Sp1 binding sites are responsible for p21 silencing. *Proceedings of the American Association for Cancer Research* (43) 2002, P 1115 (abstr 5527).

5. Ding H, **Duan W**, Zhu W, Otterson G, Villalona-Calero M. ATM participates in topoisomerase II inhibitors induced p21 expression in p53 null cell lines. *Proceedings of the American Association for Cancer Research* (43) 2002, P 627 (abstr 3113).

6. **Duan W**, Ding H, Zhu W, Zilliox L, Srinivasan K, Otterson G, Villalona-Calero M. Expression of p16 ^{ink4a} gene and p21$^{WAF1/CIP1}$ gene in lung adenocarcinomas of the SPC-p53 (273H) transgenic mice. *Proceedings of the American Association for Cancer Research* (43) 2002, P 813 (abstr 4032).

7. Villalona-Calero M, **Duan W**, Otterson G, Kleiber B, Hindman K, Shah M, Young D, Wu W, Kuhn J.. Thalidomide Modulation of Irinotecan; an NF-kB Dependent Effect? *AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics*, 2002

8. **Duan W**, Gao L, Zhu W, Otterson G, and Villalona-Calero M. In vivo expression of human mutant p53-273H does not regulate the expression of p21$^{WAF1/CIP1}$ in p53 null and heterozygous mice. *Proceedings of the American Association for Cancer Research Annual Meeting* (44) 2003, P660.

9. Zhu W, **Duan W**, Villalona-Calero M, and Otterson G. Cytotoxicity of 5-aza-2'-deoxycytidine by induction of a DNA damage response pathway. *Proceedings of the American Association for Cancer Research Annual Meeting* (44)2 003, P822.

10. Panico K, **Duan W**, Otterson G, Kleiber B, Hindman K, Shah M, Young D, Wu W, Kuhn J, Villalona-Calero M. Phase I and pharmaco-biological study of thalidomide and celecoxib as modulators of irinotecan's anti-cancer activity. *Proceedings of the AACR-NCI-EORTC International Conference, Molecular Targets and Cancer Therapeutics*, 2003, p6197 (abstr B248).

11. **Duan W**, Gao L, Druhan L, Zhu W, Otterson G, Villalona-Calero M. Over expression of Pirh2 and concomitant reduction of p53 are associated with lung adenocarcinoma.

Proceedings of the 95th Annual Meeting of the American Association for Cancer Research, 2004 (abstr 1871).

12. Gao L, **Duan W**, Zhu W, Otterson G, Villalona-Calero M. Gene dosage and aging in lung tumorigenesis in p53 (273H) transgenic mice. *Proceedings of the 95th Annual Meeting of the American Association for Cancer Research*, 2004 (abstr 2553).

13. Otterson G, Hileman T, **Duan W**, Zhu W, Villalona-Calero M. Valproic acts as an HDAC inhibitor in cells and works synergistically with the DNMT inhibitor, 5-aza-2'-deoxycytidine. *Proceedings of the 95th Annual Meeting of the American Association for Cancer Research*; 2004 (abstr 1598).

14. Villalona-Calero M, Sawada T, Fukino K, **Duan W**, Brena RM, Williams N, Plass C, Eng C. Variable responses to EGFR tyrosine kinase inhibitors in non-small cell lung cancer (NSCLC) may be due to variable somatic EGFR mutational spectra. *The third international Chicago Symposium on malignancies of the Chest and Head and Neck*. 2004.

15. **Duan W**, Gao L, Wu X, Zhang Y, Otterson G, and Villalona-Calero M. Differences between the Pirh2 and Mdm2 in Response to DNA Damage. *Proceedings of the 96th Annual Meeting of the American Association for Cancer Research*, 2005 (abstr 3639).

16. **Gao L**, Duan W, Zhang Y, Wu X, Otterson G, and Villalona-Calero M. Establishment and characterization of a line of transgenic mice harboring a lung specific human type II p53(175H) mutation. *Proceedings of the 96th Annual Meeting of the American Association for Cancer Research*, 2005 (abstr 1055).

17. Villalona-Calero MA, Bekaii-Saab T, Burak W, Ross P, Otterson G, Xu Y, Criswell T, **Duan W**, Young D, Miller J, Kolesar J. Phase II randomized study of mitomycin C (MMC) as a modulator of irinotecan in patients (pts) with esophageal and GE Junction adenocarcinomas. *Proceedings of American society of Clinical Oncology*, 2005 (abstr 4027).

18. Villalona-Calero M, **Duan W**, Gao L, Zhang Y, Wu X, Otterson G. Establishment and characterization of a line of transgenic mice harboring a lung specific human type II p53(175H) mutation: a potential model of human disease. *Proceedings of the 11th World Conference on Lung Cancer*, 2005 (abstr P-128)

19. Villalona-Calero M, **Duan W**, Gao L, Wu X, Otterson G. Establishment of Lung Cancer Transgenic Animal Models with Type Specific P53 Mutants for Experimental Therapeutics Studies. *4th International Chicago Symposium on Malignancies of the Chest and Neck & Head*, 2006 (abstr 4.04.04), pp909

20. **Duan W**, Gao L, Wu X, Otterson G, and Villalona-Calero M. Expression of a mutant p53 in lung specific transgenic mice cause an age-related demographic shift in lung tumor

incidence. *Proceedings of the 98th Annual Meeting of the American Association for Cancer Research*, 2007 (abstr 3875).

21. Gao L, **Duan W**, Wu X, Otterson G, and Villalona-Calero M. Human mutant p53 lung cancer cells respond differently to PRIMA-1 induced apoptosis. *Proceedings of the 98th Annual Meeting of the American Association for Cancer Research*, 2007 (abtr 4879).

22. Gao L, **Duan W**, Wu X, Wang L, Otterson G, and Villalona-Calero M. PRIMA-1 stabilize p53 by altering phosphorylation to induce apoptosis in human lung cancer cells. *Proceedings of the 99th Annual Meeting of the American Association for Cancer Research*, 2008 (abstr 5656).

23. **Duan W**, Gao L, Wu X, Wang L, Hade EM, Gao GX, Barsky SH, Otterson GA, Villalona-Calero M. Mutant p53 collaborating with K-ras gene mutations and p16INK4a promoter methylation result in an age-related demographic shift in spontaneous lung tumor formation in transgenic mice. *Proceedings of the 99th Annual Meeting of the American Association for Cancer Research*, 2008 (abstr 2960).

24. Otterson G, Wang L, Wu X, **Duan W**, Gao L, Karpenko M, Villalona-Calero M. Effect of dichloroacetate in combination with chemotherapy on human lung cancer cells. *J Clin Oncol* 26: 2008 (May 20 suppl; abstr 14637).

25. Wu X, Yan F, **Duan W**, Gao L, Crawford M, Nuova GJ, Nana-Sinkam P, Villalona-Calero MA, Otterson GA. MicroRNA miR205 enhances cisplatin-induced apoptosis in lung cancer cells. *Proceedings of the 100th Annual Meeting of the American Association for Cancer Research*, 2009 (abstr 1376).

26. **Duan W**, Gao L, Wu X, Cohn D, O'Malley D, Dial L, Otterson G, and Villalona-Calero M. Analysis of FANCD2 protein monoubiquitin status and nuclear foci formation in ovarian cancers. *Proceedings of the 100th Annual Meeting of the American Association for Cancer Research*, 2009 (abstr 1019).

27. Gao L, **Duan W**, Wu X, Otterson G, and Villalona-Calero M. PRIMA-1 regulates microRNA 34A to promote apoptosis in human lung cancer cells. *Proceedings of the 100th Annual Meeting of the American Association for Cancer Research*, 2009 (abstr 5586).

28. Cohn DE, **Duan W**, Leon M, Resnick K, Zhao W, Gao L, Villalona M. Assessment of the Fanconi Anemia/BRCA pathway in epithelial ovarian cancer: An exploratory analysis providing insight into the use of PARP inhibitors. *Proc Soc Gynecol Oncol 2010*.

29. Resnick K, Leon M, **Duan W**, Zhao W, Salani R, Cohn DE, Villalona-Calero M. Identification of candidates for poly(ADP-ribose) polymerase inhibition: A pilot analysis in patients with cervical cancer. *Proc Soc Gynecol Oncol 2010*.

30. **Duan W**, Gao L, Wu X, Zhao W, Leon M, Otterson G, and Villalona-Calero M. Functional analysis of the Fanconi Anemia pathway in primary lung tumors. *Proceedings of the 101 Annual Meeting of the American Association for Cancer Research*, 2010 (abstr 3750)

31. Zhao W, **Duan W**, Leon ME, Chen AP, Sofletea G, Thurmond J, Ramaswamy B, O'Malley D, Bekaii-Saab TS, Villalona MA. Targeting fanconi anemia (FA) repair pathway deficiency for treatment with PARP inhibitors. *Proceedings of American Society of Clinical Oncology*, 2010 (abstr 43623)

32. **Duan W**, Gao L, Vereb G, Wu X, Otterson G, and Villalona-Calero M. Regression of spontaneous non-small cell lung cancers in P53 mutant transgenic mice following exposure to PRIMA-1. *Cancer Res 2011*;71(8 Suppl):Abstract nr 610

33. Li Gao **Duan W**, Wu X, Otterson G, and Villalona-Calero M. Inhibition of poly(ADP-ribose) polymerase in lung cancer cells with defective Fanconi anemia (FA) pathway. *Proceedings of the 102 Annual Meeting of the American Association for Cancer Research*, 2011 (abstr 5500). 04/2011

34. **Duan W**, Gao L, Wu X, Otterson G, and Villalona-Calero M. Targeting mutant p53 in non-small cell lung cancer with PRIMA-1. *J Thorac Oncol*. 2011 6(6):S918. 08/2011

35. Ramaswamy B, Srividya V, Mullins D, Cathothers S, Young G, **Wenrui D**, Zhao W, Lustberg M, Leon M, Wesolowski R, Layman R, Mrózek E, Shapiro CL, Villalona-Calero M. 2011. Prevalence of Dysfunctional Fanconi Anemia (FA) DNA Repair Pathway in Breast Cancer. *2011 Annual Meeting of the San Antonio Breast Cancer Symposium in San Antonio Texas*. 12/2011

36. Villalona-Calero1 MA, **Duan W**, Zhao W, Gao L, Thurmond1 J, Leon1 M, Shilo K, De Fiore1 T, Westman1 JA, Ji J, Zhang Y, Marshall J, Rose1 J, Bekaii-Saab T, Chen A and Otterson G. Phase I trial of veliparib or mitomycin C + veliparib in pts with Fanconi anemia pathway (FA) repair defects. Proceedings of the AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics; 2011 Nov 12-16; San Francisco, CA. *Mol Cancer Ther 2011;10(11 Suppl):*Abstract nr A99.

37. Wu X, Yan F, **Duan W**, Zhang J, Gao L, Crawford M, Villalona M, S. Nana-Sinkam P, Otterson GA. Global miRNA expression changes induced by HDAC-42 and 5-azaCdr in lung cancer cells. *Proceedings of the 103rd Annual Meeting of the American Association for Cancer Research; 2012 Mar 31-Apr 4; Chicago, IL. Cancer Res 2012;72(8 Suppl):Abstract nr 4082.* doi:1538-7445.AM2012-4082

38. **Duan W**, Gao L, Brooks C, Kalvala A, Wu X, Otterson G, and Villalona-Calero M. Establishment of P53 mutant type specific spontaneous lung tumor in transgenic mice for treatment. In: Proceedings of the 103rd Annual Meeting of the American Association for Cancer Research; 2012 Mar 31-Apr 4; Chicago, IL. Philadelphia (PA): AACR; *Cancer Res 2*012; 72(8 Suppl):Abstract nr 4740. doi:1538-7445.AM2012-4740

39. Gao L, **Duan W**, Wu X, Chen A, Otterson G, and Villalona-Calero M. Compensatory activation of alternative DNA repair pathways following exposure to the PARP Inhibitor ABT-888 in vitro and in patients with solid malignancies. In: Proceedings of the 103rd Annual Meeting of the American Association for Cancer Research; 2012 Mar 31-Apr 4; Chicago, IL. Philadelphia (PA): AACR; *Cancer Res* 2012; 72(8 Suppl):Abstract nr 4682. doi:1538-7445.AM2012-4682

40. Villalona-Calero MA, **Duan W**, Zhao W, Shilo K, Ji J, Thurmond J, Norris A, Rose J, Layman R, Marshall J, Bekaii-Saab T, and Chen A. Phase I trial of veliparib or mitomycin (MMC) + veliparib in patients with sporadic solid tumors screened for somatic deficiency in the Fanconi Anemia (FA) pathway. In: Proceedings of the 104th Annual Meeting of the American Association for Cancer Research; 2013 Apr 6-10; Washington, DC. Philadelphia (PA): AACR; *Cancer Res* 2013; 73(8 Suppl):Abstract nr LB-139. doi:10.1158/1538-7445.AM2013-LB-139

41. Singh M, Leasure J, Chronowski C, Li N, Bondra K, **Duan W**, Villalona MA, Vergis A, Hensley L, Kaplon R, Geier B, Kurmasheva R, Woods G, Hammond S, Houghton P,. Pelloski CE. Targeting FANCD2 as a radiosensitizer in pediatric rhabdomyosarcoma. [abstract]. In: Proceedings of the 104th Annual Meeting of the American Association for Cancer Research; 2013 Apr 6-10; Washington, DC. Philadelphia (PA): AACR; *Cancer Res* 2013; 73(8 Suppl):Abstract nr 4439. doi:10.1158/1538-7445.AM2013-4439

42. **Duan W**, Rees T, Vu K, Barnwell B, Gao L, Kalvala A, Wu X, Otterson GA, Villalona-Calero MA. Promoter hypermethylation and gene expression of FANCF in non-small cell lung cancer (NSCLC). In: Proceedings of the 104th Annual Meeting of the American Association for Cancer Research; 2013 Apr 6-10; Washington, DC. Philadelphia (PA): AACR; *Cancer Res* 2013; 73(8 Suppl):Abstract nr 4246. doi:10.1158/1538-7445.AM2013-4246

43. Gao L, **Duan W**, Barnwell B, Kalvala A, Otterson GA, Villalona-Calero MA. Sensitivity of small cell lung cancer cells with defective Fanconi Anemia (FA) pathway to BCL2 inhibitors. In: Proceedings of the 104th Annual Meeting of the American Association for Cancer Research; 2013 Apr 6-10; Washington, DC. Philadelphia (PA): AACR*; Cancer Res* 2013; 73(8 Suppl):Abstract nr 4365. doi:10.1158/1538-7445.AM2013-4365

44. Kalvala A, Gao L, Barnwel B, Otterson G, Villalona Calero MA, **Duan W**. Mutations in Rad51C in colon tumors. In: Proceedings of the 104th Annual Meeting of the American Association for Cancer Research; 2013 Apr 6-10; Washington, DC. Philadelphia (PA): AACR; *Cancer Res* 2013; 73(8 Suppl):Abstract nr 4221. doi:10.1158/1538-7445.AM2013-4221

45. **Duan W**, Gao L, Kalvala A, Barnwell B, Brooks C, Mo X, Ding H, Shilo K, Otterson GA, Villalona-Calero. Type of P53 mutation influences oncogenic potential and spectrum of associated K-ras mutations in lung specific transgenic mice. *J Thorac Oncol*. 8(11Suppl 2):S738, 2013

46. Gao L, Barnwell B, Kalvala A, Otterson GA, **Duan w**, Villalona-Calero MA. Combined BCL-2/XL and mTor inhibition promotes apoptosis in small cell lung cancer. In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; 2014 Apr 5-9; San Diego, CA. Philadelphia (PA): AACR; *Cancer Res* 2014; 74(19 Suppl):Abstract nr 5434. doi:10.1158/1538-7445.AM2014-5434, 2014

47. Kalvala A, Gao L, Barnwel B, Otterson G, Villalona Calero MA, **Duan W.** Investigation of Novel Rad51c-ATXN7 fusion gene in colorectal tumors. In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; 2014 Apr 5-9; San Diego, CA. Philadelphia (PA): AACR; *Cancer Res* 2014;74(19 Suppl):Abstract nr 2407. doi:10.1158/1538-7445.AM2014-2407, 2014

48. Duan W, Gao L, Aguila B, Dotts K, Kalvala A, Webb A, Papp A, Sadee W, Otterson GA, Villalona-Calero. Genetic alterations in the Fanconi Anemia pathway in lung and colorectal cancers. *4th Global Cancer Genomics Consortium Symposium, Kyoto, Japan.* Page 18, 11/2014

49. Cui T, Srivastava AK, Han C, Zhao R, Yang L, Zou N, Qu M, **Duan W,** Zhang X, Zhao W, Wang Q. XPC inhibits NSCLC cell proliferation and migration by enhancing E-cadherin expression. *Proceedings of the 106 Annual Meeting of the American Association for Cancer Research*, 2015 (abstr 46). 04/2015

50. Kalvala A, Gao L, Dotts K, Cortes OC, Barnwel B, Otterson G, Villalona Calero MA, **Duan W.** Potential oncogenic function of Rad51C splice variant in colorectal tumors. In: Proceedings of the 106th Annual Meeting of the American Association for Cancer Research; 2015 Apr 18-22; Philadelphia, PA. Philadelphia (PA): AACR; *Cancer Res* 75(15 Suppl):Abstract nr 3866. doi:10.1158/1538-7445.AM2015-3866, 2015

51. Gao L, **Duan W**, Dotts K, Kalvala A, Aguila B, Otterson GA, Villalona-Calero MA. Inhibition of pro-survival pathways in lung cancer cells with functional defects in the Fanconi Anemia pathway. In: Proceedings of the 106th Annual Meeting of the American Association for Cancer Research; 2015 Apr 18-22; Philadelphia, PA. Philadelphia (PA): AACR; *Cancer Res* 75(15 Suppl):Abstract nr 559. doi:10.1158/1538-7445.AM2015-559, 2015

52. Duan W, Gao L, Dotts K, Kalvala A, Aguila B, Otterson GA, Villalona-Calero. Genetic alterations in the Fanconi Anemia pathway in lung cancers. 17th World Conference on Lung Cancer (WCLC 2015). September 9, 2015. Denver, CO, USA. *J Thorac Oncol*. 10(9) Suppl 2):S391, 2015

53. Fink A, Kalvala A, Gao L, Dotts K, Aguila B, Tang S, Otterson GA, Villalona MA, **Duan W**. Promoter hypermethylation status of Fanconi Anemia (FA) pathway genes FANCF, FANCL and FANCS in non-small cell lung cancer (NSCLC). In: Proceedings of the 107th Annual Meeting of the American Association for Cancer Research; 2016 Apr 16-20; New Orleans, Louisiana. Abstract # 4438

54. Mikhail S, Mousa L, Wei L, **Duan W**, Zhao W, Villalona-Calero MA, Clinical and pathological characterization of patients (pts) with functional deficiency of the fanconi anemia (FA) pathway. In Proceedings of American Society of Clinical Oncology, 2016. *J Clin Oncol* 34, 2016 (suppl; abstr e23247).

CURRENT RESEARCH PROJECTS

Project 1: ***Targeting cancer cells containing mutant p53***
p53 mutations are reported in 50-60% of non-small cell lung cancers and in up to 90% of small cell tumors, thus p53 represent a common mutation in this malignancy. Studies have shown that restoring wild type p53 function leads to regression of cancers, supporting the notion of treating human cancers by way of pharmacological reactivation of p53. The novel small molecule PRIMA-1 (p53-dependent reactivation and induction of massive apoptosis) has been shown to induce apoptosis in human tumor cells containing mutant p53. We are investigating the effects of PRIMA-1 in apoptosis using human lung cancer cell lines containing wildtype, mutant and null p53. Because most normal lung cells contain wild type p53, PRIMA-1 is expected to be much less toxic to normal lung cells compared to cancer cells. We have developed two lines of lung specific mutant p53 transgenic mice, which develop spontaneous non-small cell lung cancers. We plan to treat these lung tumor bearing mice with PRIMA-1 either as a single agent or in combination with cisplatin in order to uncover the potential role of PRIMA-1 in inducing apoptosis in spontaneous non small cell lung cancers. We are especially interested in the relationship between PRIMA-1 and microRNAs in apoptosis. This project was funded by Joan's Legacy and LUNGevity Foundation.

Project 2: ***Functional Analysis of the Fanconi Anemia (FA) pathway to select cancer treatment***
The Fanconi Anemia (FA) pathway is essential for human cells to maintain integrity following DNA damage. Twenty genes are involved in the homologous recombination repair mediated by this pathway. More recent studies provide evidences linking disruption of FA cascade in sporadic cancers. These disruptions of FA pathway may involve epigenetic silencing of the FA-core complex or mutations of one or several FA genes. Cancer cells with these defects have been shown to be more sensitive to treatment with DNA interactive chemotherapeutic agents, as well as to agents which disrupt other repair mechanisms. However, the complexity to evaluate each individual gene for genetic or epigenetic changes have prevented to take advantage of the presence of these defects to select the patients most likely to benefit from DNA breaking treatment. The development of assays that can evaluate functionality of the whole pathway would be critical to make this a practical approach. Monoubiquitylation of FancD2 protein is a critical and gene-action converging step in the activation of this pathway, leading to the repair of DNA interstrand cross-link agents induced damage. Foci on chromatin can be appreciated when the function of this pathway is spared. We are conducting research in solid tumor specimens from patients undergoing surgical procedures to evaluate for an all inclusive method assessing the functionality of the Fanconi Anemia pathway. This test could potentially lead to the identification of patients most likely to respond to DNA breaking agents or to agents inhibiting compensatory mechanisms of repair. This project was funded by NCI research grant.

Project 3: ***Genetic and epigenetic alterations in human lung cancer***

A major mechanism of DNA repair related to homologous recombination is the Fanconi Anemia (FA) pathway. FA genes collaborate with BRCA genes to form foci of DNA repair on chromatin following DNA damage or during S phase of cell cycle. Lack of repair foci and BRCA gene (BRCA1 or BRCA2) deficiency have been identified as predictors of the cytotoxicity of DNA breaking agents respectively. Although the numbers of cancer patients with germ line BRCA deficiency are low, BRCA genes are two of many genes that collaborate in the FA pathway. More recent studies provide evidence linking disruption of FA/BRCA cascade in sporadic cancers. However, more than 20 genes are actively involved in the FA pathway and both genetic and epigenetic alterations can occur. The aggregate contribution of these genes results first in activation and FANCD2 followed by the formation of FANCD2 repair foci in the nucleus of proliferating cells. We have recently developed a FA triple staining immunofluorescence based method (FATSI) to evaluate FANCD2 foci formation, which is capable of evaluating the presence or absence of FANCD2 foci using formalin fixed paraffin embedded (FFPE) tumor samples, and have generated preliminary data showing somatic deficiency of this pathway in tumors across several organ sites that include lung cancers. However, the specific genetic and epigenetic alterations that lead to inactivation of FA pathway in these sporadic tumors and the potential implication of these changes related to treatment are still unknown. We hypothesize that a substantial proportion of lung tumor harbors somatic genetic or epigenetic alterations resulting in defective FA homologous recombination repair. In order to provide molecular evidence that will help us to understand FA pathway inactivation in lung cancer, we propose to accomplish the following research aims:1) To identify FANCD2 foci defective tumor in lung cancer patients by analyzing human lung tumor and matching non-tumor samples; 2) To perform a functional genomics analysis of FANCD2 foci defective tumors identified in aim 1 through analysis of the RNA transcriptome associated with the FA pathway in the tumor and adjacent non-tumor tissues, using next generation sequencing (RNAseq), 3) To investigate promoter methylation of FA genes in FANCD2 foci defective tumors identified in aim 1. This project was supported by NCI research grant and American Cancer Society research grant.