



## EPIZYME SCIENTIFIC PUBLICATIONS REFERENCE

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### 2009 Publications

1. Anderson TR, Bell JE, Bond JS, Boyer R, Copeland RA, Gordon B, Kresge N, Rubinstein PA, Wolfson AJ. **The Biochemistry and Molecular Biology Major and Liberal Education.** Liberal Education. 2009;95: 6-13.
2. Copeland RA. **Molecularly targeted cancer therapy.** Special Edition Drug Discovery Today: Therapeutic Strategies, Cancer. 2009;6:45-6.
3. Pollock RM, Richon VM. **Epigenetic approaches to cancer therapy.** Drug Discovery Today: Therapeutic Strategies. 2009;6(2):71-9.
4. Copeland RA, Solomon ME, Richon VM. **Protein methyltransferases as a target class for drug discovery.** Nat Rev Drug Discov. 2009 Sep;8(9):724-32.

### 2010 Publications

5. Copeland RA. **The dynamics of drug-target interactions: drug-target residence time and its impact on efficacy and safety.** Expert Opin Drug Discov. 2010 Apr;5(4):305-10.
6. Richon VM. **Targeting histone deacetylases: development of vorinostat for the treatment of cancer.** Epigenomics. 2010 Jun;2(3):457-65.
7. Copeland RA, Olhava EJ, Porter Scott M. **Targeting epigenetic enzymes for drug discovery.** Curr Opin Chem Biol. 2010 Aug;14(4):505-10.
8. Sneeringer CJ, Porter Scott M, Kuntz KW, Knutson SK, Pollock RM, Richon VM, Copeland RA. **Coordinated activities of wild-type plus mutant EZH2 drive tumor-associated hypertrimethylation of lysine 27 on histone H3 (H3K27) in human B-cell lymphomas.** Proc Natl Acad Sci U S A. 2010 Dec 7;107(49):20980-5.

### 2011 Publications

9. Wigle TJ. **Promoting Illiteracy in Epigenetics: An Emerging Therapeutic Strategy.** Curr Chem Genomics. 2011;5(Suppl 1):48-50.
10. Daigle SR, Olhava EJ, Therkelsen CA, Majer CR, Sneeringer CJ, Song J, Johnston LD, Porter Scott M, Smith JJ, Xiao Y, Jin L, Kuntz KW, Chesworth R, Moyer MP, Bernt KM, Tseng J-C, Kung AL, Armstrong SA, Copeland RA, Richon VM, Pollock RM. **Selective Killing of Mixed Lineage Leukemia Cells by a Potent Small-Molecule DOT1L Inhibitor.** Cancer Cell. 2011 Jul 12;20(1):53-65.

11. Bernt KM, Zhu N, Sinha AU, Vempati S, Faber J, Krivtsov AV, Feng Z, Punt N, Daigle A, Bullinger L, Pollock RM, Richon VM, Kung AL, Armstrong SA. **MLL-Rearranged Leukemia Is Dependent on Aberrant H3K79 Methylation by DOT1L.** *Cancer Cell.* 2011 Jul 12;20(1):66-78.
12. Richon VM, Johnston D, Sneeringer CJ, Jin L, Majer CR, Elliston K, Jerva LF, Porter Scott M, Copeland RA. **Chemogenetic Analysis of Human Protein Methyltransferases.** *Chem Biol Drug Des.* 2011 Aug;78(2):199-210.
13. Copeland RA. **Conformational adaptation in drug-target interactions and residence time.** *Future Med Chem.* 2011 Sep;3(12):1491-501.
14. Copeland RA, Basavapathruni A, Moyer M, Porter Scott M. **Impact of enzyme concentration and residence time on apparent activity recovery in jump dilution analysis.** *Anal Biochem.* 2011 Sep 15;416(2):206-10.
15. Wigle TJ, Knutson SK, Jin L, Kuntz KW, Pollock RM, Richon VM, Copeland RA, Porter Scott M. **The Y641C mutation of EZH2 alters substrate specificity for histone H3 lysine 27 methylation states.** *FEBS Lett.* 2011 Oct 3;585(19):3011-4.

## 2012 Publications

16. Copeland RA. **Disease-Driving Genes and Molecules to Target Them Create the Promise of Personalized Therapeutics.** (2012) Sponsor's Foreword for Nature Reprint Collection: Epigenetics, Nature Publishing Group, [www.nature.com/reprintcollectuins/epigenetics](http://www.nature.com/reprintcollectuins/epigenetics).
17. Copeland RA. **Protein methyltransferase inhibitors as personalized cancer therapeutics.** *Drug Discov. Today: Therapeutic Strategies.* 2012;9:83-90.
18. Richon VM, Moyer MP & Copeland RA. (2012). **Protein Methyltransferases as Targets for Personalized Cancer Therapeutics.** *American Association for Cancer Research Annual Meeting 2012 Education Book* (pp. 107-112). Philadelphia: AACR.
19. Majer CR, Jin L, Porter Scott M, Knutson SK, Kuntz KW, Keilhack H, Smith JJ, Moyer MP, Richon VM, Copeland RA, Wigle TJ. **A687V EZH2 is a gain-of-function mutation found in lymphoma patients.** *FEBS Lett.* 2012 Sep 21;586(19):3448-51.
20. Knutson SK, Wigle TJ, Warholc NM, Sneeringer CJ, Allain CJ, Klaus CR, Sacks JD, Raimondi A, Majer CR, Song J, Porter Scott M, Jin L, Smith JJ, Olhava EJ, Chesworth R, Moyer MP, Richon VM, Copeland RA, Keilhack H, Pollock RM, Kuntz KW. **A selective inhibitor of EZH2 blocks H3K27 methylation and kills mutant lymphoma cells.** *Nat Chem Biol.* 2012 Nov;8(11):890-6.
21. Basavapathruni A, Jin L, Daigle SR, Majer CR, Therkelsen CA, Wigle TJ, Kuntz KW, Chesworth R, Pollock RM, Scott MP, Moyer MP, Richon VM, Copeland RA, Olhava EJ. **Conformational Adaptation Drives Potent, Selective and Durable Inhibition of the Human Protein Methyltransferase DOT1L.** *Chem Biol Drug Des.* 2012 Dec;80(6):971-80.

## 2013 Publications

22. Copeland RA: **"Enzymology in Drug Discovery: Part 1 of 2"** (2013) In: Small Molecule Drug Discovery (M. R. Arkin, Ed.) The Biomedical & Life Sciences Collection, Henry Stewart Talks, Ltd, London.
23. Copeland RA: **"Enzymology in Drug Discovery: Part 2 of 2"** (2013) In: Small Molecule Drug Discovery (M. R. Arkin, Ed.) The Biomedical & Life Sciences Collection, Henry Stewart Talks, Ltd, London.
24. Copeland RA, Moyer MP, Richon VM. **Targeting genetic alterations in protein methyltransferases for personalized cancer therapeutics.** *Oncogene*. 2013 Feb 21;32(8):939-46.
25. Deshpande AJ, Chen L, Fazio M, Sinha AU, Bernt KM, Banka D, Dias S, Chang J, Olhava EJ, Daigle SR, Richon VM, Pollock RM, Armstrong SA. **Leukemic transformation by the MLL-AF6 fusion oncogene requires the H3K79 methyltransferase Dot1L.** *Blood*. 2013 Mar 28;121(13):2533-41.
26. Chen L, Deshpande AJ, Banka D, Bernt KM, Dias S, Buske C, Olhava EJ, Daigle SR, Richon VM, Pollock RM, Armstrong SA. **Abrogation of MLL-AF10 and CALM-AF10-mediated transformation through genetic inactivation or pharmacological inhibition of the H3K79 methyltransferase Dot1L.** *Leukemia*. 2013 Apr;27(4):813-22.
27. Knutson SK, Warholic NM, Wigle TJ, Klaus CR, Allain CJ, Raimondi A, Porter Scott M, Chesworth R, Moyer MP, Copeland RA, Richon VM, Pollock RM, Kuntz KW, Keilhack H. **Durable tumor regression in genetically altered malignant rhabdoid tumors by inhibition of methyltransferase EZH2.** *Proc Natl Acad Sci U S A*. 2013 May 7;110(19):7922-7.
28. Wigle TJ, Copeland RA. **Drugging the human methylome: an emerging modality for reversible control of aberrant gene transcription.** *Curr Opin Chem Biol*. 2013 Jun;17(3):369-78.
29. Swalm BM, Hallenbeck KK, Majer CR, Jin L, Scott MP, Moyer MP, Copeland RA, Wigle TJ. **Convergent evolution of chromatin modification by structurally distinct enzymes: comparative enzymology of histone H3 Lys<sup>27</sup> methylation by human polycomb repressive complex 2 and vSET.** *Biochem J*. 2013 Jul 15;453(2):241-7.
30. Daigle SR, Olhava EJ, Therkelsen CA, Basavapathruni A, Jin L, Boriack-Sjodin PA, Allain CJ, Klaus CR, Raimondi A, Porter Scott M, Waters NJ, Chesworth R, Moyer MP, Copeland RA, Richon VM, Pollock RM. **Potent inhibition of DOT1L as treatment of MLL-fusion leukemia.** *Blood*. 2013 Aug 8;122(6):1017-25.
31. Copeland RA. **Molecular Pathways: Protein Methyltransferases in Cancer.** *Clin. Cancer Res*. 2013 Dec 1; 19: 6344-6350.

## 2014 Publications

32. Richon VM, Moyer MP, & Copeland RA. (2014). **Targeting Chromatin Modifying Enzymes in Anti-Cancer Drug Discovery**. In: A. Emili, J. Greenblatt & S. Wodak (Eds.), *Systems Analysis of Chromatin-Related Protein Complexes in Cancer* (pp. 239-256). New York: Springer.
33. Waters NJ, Obach RS, Di L. **Consideration of the Unbound Drug Concentration in Enzyme Kinetics**. *Methods Mol Biol*. 2014;1113:119-45.
34. Wee S, Dhanak D, Li H, Armstrong SA, Copeland RA, Sims R, Baylin SB, Liu XS, Schweizer L. **Targeting Epigenetic Regulators for Cancer Therapy**. *Annals of the New York Academy of Sciences*. 2014;1309:30-6.
35. Knutson SK, Kawano S, Minoshima Y, Warholic NM, Huang KC, Xiao Y, Kadowaki T, Uesugi M, Kuznetsov G, Kumar N, Wigle TJ, Klaus CR, Allain CJ, Raimondi A, Waters NJ, Smith JJ, Porter-Scott M, Chesworth R, Moyer MP, Copeland RA, Richon VM, Uenaka T, Pollock RM, Kuntz KW, Yokoi A, Keilhack H. **Selective Inhibition of EZH2 by EPZ-6438 Leads to Potent Antitumor Activity in EZH2-Mutant Non-Hodgkin Lymphoma**. *Mol Cancer Ther*. 2014 Apr;13(4):842-54.
36. Basavapathruni A, Olhava EJ, Daigle SR, Therkelsen CA, Jin L, Boriack-Sjodin PA, Allain CJ, Klaus CR, Raimondi A, Porter Scott M, Dovletoglou A, Richon VM, Pollock RM, Copeland RA, Moyer MP, Chesworth R, Pearson PG, Waters NJ. **Nonclinical pharmacokinetics and metabolism of EPZ-5676, a novel DOT1L histone methyltransferase inhibitor**. *Biopharm Drug Dispos*. 2014 May;35(4):237-52.
37. Finley A, Copeland RA. **Small Molecule Control of Chromatin Remodeling**. *Chem Biol*. 2014 Sep 18;21(9):1196-210.
38. Klaus CR, Iwanowicz D, Johnston D, Campbell CA, Smith JJ, Moyer MP, Copeland RA, Olhava EJ, Scott MP, Pollock RM, Daigle SR, Raimondi A. **DOT1L Inhibitor EPZ-5676 Displays Synergistic Antiproliferative Activity in Combination with Standard of Care Drugs and Hypomethylating Agents in MLL-Rearranged Leukemia Cells**. *J Pharmacol Exp Ther*. 2014 Sep;350(3):646-56.
39. Swalm BM, Knutson SK, Warholic NM, Jin L, Kuntz KW, Keilhack H, Smith JJ, Pollock RM, Moyer MP, Porter Scott M, Copeland RA, Wigle TJ. **Reaction Coupling between Wild-Type and Disease-Associated Mutant EZH2**. *ACS Chem Biol*. 2014 Nov 21;9(11):2459-64.
40. Knutson SK, Warholic NM, Johnston LD, Klaus CR, Wigle TJ, Iwanowicz D, Littlefield BA, Porter-Scott M, Smith JJ, Moyer MP, Copeland RA, Pollock RM, Kuntz KW, Raimondi A, Keilhack H. **Synergistic Anti-Tumor Activity of EZH2 Inhibitors and Glucocorticoid Receptor Agonists in Models of Germinal Center Non-Hodgkin Lymphomas**. *PLOS ONE*. 2014 Dec 10;9(12):e111840.

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41. Copeland RA. (2015). **Drug-Target Residence Time**. In: G. Keseru and D. C. Swinney (Eds.), *Kinetics and Thermodynamics of Drug Binding* (pp.157-167). Weinheim, Germany: Wiley-VCH.
42. Campbell JE, Kuntz KW, Knutson SK, Warholc NM, Keilhack H, Wigle TJ, Raimondi A, Klaus CR, Rioux N, Yokoi A, Kawano S, Minoshima Y, Choi HW, Porter Scott M, Waters NJ, Smith JJ, Chesworth R, Moyer MP, Copeland RA. **EPZ011989, A Potent, Orally-Available EZH2 Inhibitor with Robust in Vivo Activity**. *ACS Med Chem Lett*. 2015 Mar 4;6(5):491-5.
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44. Kühn MW, Hadler MJ, Daigle SR, Koche RP, Krivtsov AV, Olhava EJ, Caligiuri MA, Huang G, Bradner JE, Pollock RM, Armstrong SA. **MLL partial tandem duplication leukemia cells are sensitive to small molecule DOT1L inhibition**. *Haematologica*. 2015 May;100(5):e190-3.
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46. Keilhack H, Smith JJ. **Small molecule inhibitors of EZH2: the emerging translational landscape**. *Epigenomics*. 2015 Jun;7(3):337-41.
47. Waters NJ. **Evaluation of drug-drug interactions for oncology therapies: in vitro-in vivo extrapolation model-based risk assessment**. *Br J Clin Pharmacol*. 2015 Jun;79(6):946-58.
48. Copeland RA. **Drug-target interactions: Stay tuned**. *Nat Chem Biol*. 2015 Jul;11(7):451-2.
49. Rioux N, Mitchell LH, Tiller P, Plant K, Shaw J, Frost K, Ribich S, Moyer MP, Copeland RA, Chesworth R, Waters NJ. **Structural and Kinetic Characterization of a Novel N-acetylated Aliphatic Amine Metabolite of the PRMT Inhibitor, EPZ011652**. *Drug Metab Dispos*. 2015 Jul;43(7):936-43.
50. Wigle TJ, Swinger KK, Campbell JE, Scholle MD, Sherrill J, Admirand EA, Boriack-Sjodin PA, Kuntz KW, Chesworth R, Moyer MP, Porter Scott M, Copeland RA. **A High-Throughput Mass Spectrometry Assay Coupled with Redox Activity Testing Reduces Artifacts and False Positives in Lysine Demethylase Screening**. *J Biomol Screen*. 2015 Jul;20(6):810-20.

51. Arrowsmith CH, Audia JE, Austin C, Baell J, Bennett J, Blagg J, Bountra C, Brennan PE, Brown PJ, Bunnage ME, Buser-Doepner C, Campbell RM, Carter AJ, Cohen P, Copeland RA, Cravatt B, Dahlin JL, Dhanak D, Edwards AM, Frye SV, Gray N, Grimshaw CE, Hepworth D, Howe T, Huber KVM, Jin J, Knapp S, Kotz JD, Kruger RG, Lowe D, Mader MM, Marsden B, Mueller-Fahrnow A, Müller S, O'Hagan RC, Overington JP, Owen DR, Rosenberg SH, Roth B, Ross R, Schapira M, Schreiber SL, Shoichet B, Sundström M, Superti-Furga G, Taunton J, Toledo-Sherman L, Walpole C, Walters MA, Willson TM, Workman P, Young RN, Zuercher WJ. **The Promise and Peril of Chemical Probes.** Nat Chem Biol. 2015 July 21;11(8):536-541.
52. Waters NJ, Daigle SR, Rehlaender BN, Basavapathruni A, Campbell CT, Jensen TB, Truitt BF, Olhava EJ, Pollock RM, Stickland KA, Dovletoglou KA. **Exploring drug delivery for the DOT1L inhibitor pinometostat (EPZ-5676): subcutaneous administration as an alternative to continuous IV infusion, in the pursuit of an epigenetic targets.** J Control Release. 2015 Sept 15;220:758-65.
53. Grassian AR, Scales TME, Knutson SK, Kuntz KW, McCarthy NJ, Lowe CE, Moore JD, Copeland RA, Keilhack H, Smith JJ, Wichenden JA, Ribich S. **A Medium-Throughput Single Cell CRISPR-Cas9 Assay to Assess Gene Essentiality.** Biol Proced Online. 2015 Nov 14;17:15.
54. Duncan KW, Rioux N, Boriack-Sjodin PA, Munchhof MJ, Reiter LA, Majer CR, Jin L, Johnston LD, Chan-Penebre E, Kuplast KG, Porter Scott M, Pollock RM, Waters NJ, Smith JJ, Moyer MP, Copeland RA, Chesworth R. **Structure and Property Guided Design in the Identification of PRMT5 Tool Compound EPZ015666.** ACS Med Chem Lett. 2015 Dec 2;7(2):162-6.

## 2016 Publications

55. Boriack-Sjodin PA. **Epigenetic Proteins as Emerging Drug Targets.** *Structural Biology in Drug Discovery: Methods, Techniques, and Practices.* 2016 in press.
56. Boriack-Sjodin A, Swinger KK. **Protein Methyltransferases: A Distinct, Diverse, and Dynamic Family of Enzymes.** Biochemistry. 2016;55(11):1557-69.
57. Copeland RA. **Epigenetic Medicinal Chemistry.** ACS Med Chem Lett. 2016;7(2):124-7.
58. Copeland RA, & Boriack-Sjodin PA. (2016). **Enzyme Inhibitors: Biostructure-Based and Mechanism-Based Design.** In: U. Madsen, P. Krosggaard-Larsen, & K. Stromgaard (Eds.), *Textbook of Drug Design and Discovery, 5<sup>th</sup> Edition* (pp. 175-191). New York: CRC Press.
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62. Kuntz KW, Campbell JE, Keilhack H, Pollock RM, Knutson SK, Scott MP, Richon VM, Sneeringer CJ, Wigle TJ, Allain CJ, Majer CR, Moyer MP, Copeland RA, Chesworth R. **The Importance of Being Me: Magic Methyls, Methyltransferase Inhibitors and the Discovery of Tazemetostat**. *J Med Chem*. 2016;59(4):1556-64.
63. Mitchell LH, Boriack-Sjodin PA, Smith S, Thomenius M, Rioux N, Munchhof M, Mills JE, Klaus C, Totman J, Riera TV, Raimondi A, Jacques SL, West K, Foley M, Waters NJ, Kuntz KW, Wigle TJ, Scott MP, Copeland RA, Smith JJ, Chesworth R. **Novel Oxindole Sulfonamides and Sulfamides: EPZ031686, the First Orally Bioavailable Small Molecule SMYD3 Inhibitor**. *ACS Med Chem Lett*. 2016;7(2):134-8.
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66. Waters NJ, Smith SA, Olhava EJ, Duncan KW, Burton RD, O'Neill J, Rodrique M, Pollock RM, Moyer MP, Chesworth R. **Metabolism and disposition of the DOT1L inhibitor, pinometostat (EPZ-5676), in rat, dog and human**. *Cancer Chemother Pharmacol*. 2016 Jan;77(1):43-62.
67. Copeland RA. **The Biochemistry of Chromatin Remodeling**. *Biochemistry*. 2016 Jan 8;55(11):1555-6.
68. Copeland RA. **The drug-target residence time model: a 10-year retrospective**. *Nature Reviews*. 2016 Feb 15;87-95.
69. Boriack-Sjodin PA, Jin L, Jacques SL, Drew A, Sneeringer C, Scott MP, Moyer MP, Ribich S, Moradei O, Copeland RA. **Structural Insights into Ternary Complex Formation of Human CARM1 with Various Ligands**. *ACS Chem Biol*. 2016 Mar 18;11(3):763-71.
70. Basavapathruni A, Gureasko J, Scott MP, Hermans W, Godbole A, Leland PA, Boriack-Sjodin PA, Wigle TJ, Copeland RA, Riera TV. **Characterization of the Enzymatic Activity of SETDB1 and its 1:1 Complex with AFT7IP**. *Biochemistry*. 2016 Mar 22;55(11):1645-51.
71. Jacques SL, Aquino KP, Gureasko J, Boriack-Sjodin PA, Scott MP, Copeland RA, Riera TV. **CARM1 Preferentially Methylates H3R17 over H3R26 Through a Random Kinetic Mechanism**. *Biochemistry*. 2016 Mar 22;55(11):1635-44.



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73. Thomenius M, Janzen W. **Epigenetic Modulators of Histone Methylation.** *Drug Discovery World*. Summer 2016.
74. Kawano S, Grassian A, Tsuda M, Knuston SK, Warholic NM, Kuznetsov G, Xu S, Xiao Y, Pollock RM, Smith JS, Kuntz KK, Ribich S, Minoshima Y, Matsui J, Copeland RA, Tanaka S, Keilhack H. **Preclinical Evidence of Anti-Tumor Activity Induced by EZH2 Inhibition in Human Models of Synovial Sarcoma.** *PLoS One*. 2016 Jul 8;11(7):e0158888.