

## **NExT Discovery Project Publications**

### **AAA ATPase p97:**

#### **Allosteric p97 Inhibitors Can Overcome Resistance to ATP-Competitive p97 Inhibitors for Potential Anticancer Therapy.**

Wang F, Li S, Gan T, Stott GM, Flint A, Chou TF. *ChemMedChem*. 2020 Apr 20;15(8):685-694. doi: 10.1002/cmdc.201900722. Epub 2020 Mar 23. PMID: 32162487.

#### **p97: An Emerging Target for Cancer, Neurodegenerative Diseases, and Viral Infections.**

Huryn DM, Kornfilt DJP, Wipf P. *J Med Chem*. 2020 Mar 12;63(5):1892-1907. doi:10.1021/acs.jmedchem.9b01318. Epub 2019 Oct 9.

#### **Optimization of Phenyl Indole Inhibitors of the AAA+ ATPase p97.**

LaPorte MG, Burnett JC, Colombo R, Bulfer SL, Alvarez C, Chou TF, Neitz RJ, Green N, Moore WJ, Yue Z, Li S, Arkin MR, Wipf P, Huryn DM. *ACS Med Chem Lett*. 2018;9(11):1075-1081.

#### **The p97 Inhibitor CB-5083 Is a Unique Disrupter of Protein Homeostasis in Models of Multiple Myeloma.**

Le Moigne R, Aftab BT, Djakovic S, Dhimolea E, Valle E, Murnane M, King EM, Soriano F, Menon M-K, Wu ZY, Wong ST, Lee GJ, Yao B, Wiita AP, Lam C, Rice J, Wang J, Chesi M, Bergsagel PL, Kraus M, Driessen C, von Soly SK, Yakes FM, Wustrow D, Shawver L, Zhou H-J, Martin TG 3rd, Wolf JL, Mitsiades CS, Anderson DJ, Rolfe R. *Mol Cancer Ther*. 2017;16(11):2375-2386.

#### **A threonine turnstile defines a dynamic amphiphilic binding motif in the AAA ATPase p97 allosteric binding site.**

Burnett JC, Lim C, Peyser BD, Samankumara LP, Kovaliov M, Colombo R, Bulfer SL, LaPorte MG, Hermone AR, McGrath CF, Arkin MR, Gussio R, Huryn DM, Wipf P. *Org Biomol Chem*. 2017;15:4096.

#### **Allosteric Indole Amide Inhibitors of p97: Identification of a Novel Probe of the Ubiquitin Pathway.**

Alvarez C, Bulfer SL, Chakrasali R, Chimenti MS, Deshaies RJ, Green N, Kelly M, LaPorte MG, Lewis TS, Liang M, Moore WJ, Neitz RJ, Peshkov VA, Walters MA, Zhang F, Arkin MA, Wipf P, Huryn DM. *ACS Med Chem Lett*. 2016;7(2):182-187.

#### **2.3 Å resolution cryo-EM structure of human p97 and mechanism of allosteric inhibition.**

Banerjee S, Bartesaghi A, Merk A, Rao P, Bulfer SL, Yan Y, Green N, Mroczkowski B, Neitz RJ, Wipf P, Falconieri V, Deshaies RJ, Milne JL, Huryn D, Arkin M, Subramaniam S. *Science*. 2016;351(6275):871-875.

#### **Structure-Activity Study of Bioisosteric Trifluoromethyl and Pentafluorosulfanyl Indole Inhibitors of the AAA ATPase p97.**

Alvarez C, Arkin MR, Bulfer SL, Colombo R, Kovaliov M, LaPorte MG, Lim C, Liang M, Moore WJ, Neitz RJ, Yan Y, Yue Z, Huryn DM, Wipf P. *ACS Med Chem Lett*. 2015;6(12):1225-30.

#### **Evaluating p97 inhibitor analogues for their domain selectivity and potency against the p97-p47 complex.**

Fang CJ, Gui L, Zhang X, Moen DR, Li K, Frankowski KJ, Lin HJ, Schoenen FJ, Chou TF. *ChemMedChem*. 2015 Jan;10(1):52-6. doi: 10.1002/cmdc.201402420. Epub 2014 Nov 6.

#### **Altered cofactor regulation with disease-associated p97/VCP mutations.**

Zhang X, Gui L, Zhang X, Bulfer SL, Sanghez V, Wong DE, Lee Y, Lehmann L, Lee, JS, Shih PY, Lin HJ, Iacovino M, Weihl CC, Arkin MR, Wang Y, Chou TF. *Proc Natl Acad Sci U S A*. 2015;112, E1705-14.

#### **A Fragment-Based Ligand Screen against Part of a Large Protein Machine: The ND1 Domains of the AAA+ ATPase p97/VCP.**

Chimenti MS, Bulfer SL, Neitz RJ, Renslo AR, Jacobson MP, James TL, Arkin MR, Kelly MJ. *J Biomol Screen*. 2015;20(6):788-800.

#### **Specific inhibition of p97/VCP ATPase and kinetic analysis demonstrate interaction between D1 and D2 ATPase domains.**

Chou T-F, Bulfer SL, Weihl CC, Li K, Lis LG, Walters MA, Schoenen FJ, Lin HJ, Deshaies RJ, Arkin MR. *J Mol Biol*. 2014;426(15):2886-2899.

#### **Structure-activity relationship study reveals ML240 and ML241 as potent and selective inhibitors of p97 ATPase.**

Chou TF, Li K, Frankowski KJ, Schoenen FJ, Deshaies RJ. *ChemMedChem*. 2013 Feb;8(2):297-312. doi: 10.1002/cmdc.201200520. Epub 2013 Jan 11.

### **Patents:**

Phenylindole derivatives as allosteric inhibitors of p97 ATPase and their preparation, WO 2017070320 A1. Apr 27, **2017**.

Preparation of alkynyl substituted triazoles as modulators of p97 AAA ATPase activity, WO 2017197080 A1. Nov 16, **2017**.

Phenyl Indole Allosteric Inhibitors of p97. Provisional patent application filed: October 21, **2015**.

### **Artemis Endonuclease:**

#### **Structural analysis of the catalytic domain of Artemis endonuclease/SNM1C reveals distinct structural features.**

Karim F, Liu S, Laciak AR, Volk L, Rosenblum M, Lieber MR, Wu M, Curtis R, Huang N, Carr G, Zhu G. *J. Biol. Chem.* **2020** Aug 28; 295(35): 12368-12377. doi: 10.1074/jbc.RA120.014136. Epub 2020 Jun 23.

#### **Evidence that the DNA endonuclease ARTEMIS also has intrinsic 5'-exonuclease activity.**

Li S, Chang HH, Niewolik D, Hedrick MP, Pinkerton AB, Hassig CA, Schwarz K, Lieber MR. *J. Biol. Chem.* **2014** Mar 14;289(11):7825-34. doi: 10.1074/jbc.M113.544874. Epub 2014 Feb 5.

### **GBM-PPI:**

#### **Disrupting the PIKE-A/Akt interaction inhibits glioblastoma cell survival, migration, invasion and colony formation.**

Qi Q, He K, Liu X, Pham C, Meyerkord C, Fu H, Ye K. *Oncogene.* **2013**;32(8):1030-40.

### **IDH1:**

#### **Discovery and optimization of 2H-1 $\lambda$ <sup>2</sup>-pyridin-2-one inhibitors of mutant isocitrate dehydrogenase 1 for the treatment of cancer.**

Rohde J, Karavathi S, Liu L, Pragani R, McIver A, Davis M, Urban D, Brimacombe K, Lee T, Yasgar A, Cheff D, Covey J, Klumpp-Thomas C, Michael S, Moore W, Boxer M, Stott G, Li Z, Simeonov A, Jadhav A, Frye S, Hall M, Zhang W, Wang X, Patnaik S, Shen M. *J Med Chem.* **2021** Apr 22; 64(8):4913-4946. doi: 10.1021/acs.jmedchem.1c00019. Epub 2021 Apr 6.

#### **Assessing inhibitors of mutant isocitrate dehydrogenase using a suite of pre-clinical discovery assays.**

Urban DJ, Martinez NJ, Davis MI, Brimacombe KR, Cheff DM, Lee TD, Henderson MJ, Titus SA, Pragani R, Rohde JM, Liu L, Fang Y, Karavathi S, Shah P, Lee OW, Wang A, McIver A, Zheng H, Wang X, Xu X, Jadhav A, Simeonov A, Shen M, Boxer MB, Hall MD. *Sci Rep.* **2017**;7(1):12758. doi: 10.1038/s41598-017-12630-x

### **Patents:**

Mutant IDH1 inhibitors useful for treating cancer. PCT/US2015/067406. filed December 22, **2015**.

### **KDM5:**

#### **KDM5 histone demethylases repress immune response via suppression of STING.**

Wu L, Cao J, Cai WL, Lang SM, Horton JR, Jansen DJ, Liu ZZ, Chen JF, Zhang M, Mott BT, Pohida K, Rai G, Kales SC, Henderson MJ, Hu X, Jadhav A, Maloney DJ, Simeonov A, Zhu S, Iwasaki A, Hall MD, Cheng X, Shadel GS, Yan Q. *PLoS Biol.* **2018**;16(8):e2006134.

#### **Insights into the action of inhibitor enantiomers against histone lysine demethylase 5A.**

Horton John, Liu X, Wu L, Zhang K, Shanks J, Zhang X, Rai G, Mott B, Jansen D, Kales S, Henderson M, Pohida K, Fang Y, Hu X, Jadhav A, Maloney D, Hall M, Simeonov A, Fu H, Vertino PM, Yan Q, Cheng X. *J Med Chem.* **2018**;61(7):3193-3208.

#### **Characterization of a linked Jumonji domain of the KDM5/JARID1 family of histone H3 lysine 4 demethylases.**

Horton JR, Engstrom A, Zoeller EL, Liu X, Shanks JR, Zhang X, Johns MA, Vertino PM, Fu H, Cheng X. *J Med Chem.* **2016**;291(6):2631-2646.

### **Structural basis for KDM5A histone lysine demethylase inhibition by diverse compounds.**

Horton J, Liu X, Gale M, Wu L, Shanks J, Zhang X, Webber P, Bell J, Kales S, Mott B, Rai G, Jansen D, Henderson M, Urban D, Hall M, Simeonov A, Maloney D, Johns M, Fu H, Jadhav A, Vertino P, Yan Q, Cheng X. *Cell Chem Biol.* **2016**;23(7):769-781.

### **LDHA:**

#### **Optimization of ether and aniline based inhibitors of lactate dehydrogenase.**

Christov PP, Kim K, Jana S, Romaine IM, Rai G, Mott BT, Allweil AA, Lamers A, Brimcombe KR, Urban DJ, Lee TD, Hu X, Lukacs CM, Davies DR, Jadhav A, Hall MD, Green N, Moore WJ, Stott GM, Flint AJ, Maloney DJ, Sulikowski GA, Waterson AG. *Bioorg Med Chem Lett.* **2021** Jun 1;41:127974. doi: 10.1016/j.bmcl.2021.127974. Epub 2021 Mar 24.

#### **Pyrazole-Based Lactate Dehydrogenase Inhibitors with Optimized Cell Activity and Pharmacokinetic Properties.**

Rai G, Urban DJ, Mott BT, Hu X, Yang SM, Benavides GA, Johnson MS, Squadrito GL, Brimacombe KR, Lee TD, Cheff DM, Zhu H, Henderson MJ, Pohida K, Sulikowski GA, Dranow DM, Kabir MD, Shah P, Padilha E, Tao D, Fang Y, Christov P, Kim K, Jana S, Muttill P, Anderson T, Kunda NK, Hathaway HJ, Kusewitt DF, Oshima N, Cherukuri M, Davies DR, Norenberg JP, Sklar LA, Moore WJ, Dang CV, Stott GM, Neckers L, Flint AJ, Darley-Usmar VM, Simeonov A, Waterson AG, Jadhav A, Hall MD, Maloney DJ. *J Med Chem.* **2020** Oct 8;63(19):10984-11011. doi: 10.1021/acs.jmedchem.0c00916. Epub 2020 Sep 27.

#### **Lactate dehydrogenases inhibition synergizes with IL-21 to promote CD8+ T cell stemness and antitumor immunity.**

Hermans D, Gautam S, García-Cañaveras JC, Gromer D, Mitra S, Spolski R, Li P, Christensen S, Nguyen R, Lin J-X, Oh J, Du N, Veenbergen S, Fioravanti J, Ebina-Shibuya R, Bleck C, Neckers LM, Rabinowitz JD, Gattinoni L, Leonard WJ. *PNAS.* **2020**;117(11):6047-6055. doi:10.1073/pnas.1920413117. Epub 2020 Mar 2.

#### **Dynamic Imaging of LDH Inhibition in Tumors Reveals Rapid In Vivo Metabolic Rewiring and Vulnerability to Combination Therapy.**

Oshima N, Ishida R, Kishimoto S, Beebe K, Brender JR, Yamamoto K, Urban D, Rai G, Johnson MS, Benavides G, Squadrito GL, Crooks D, Jackson J, Joshi A, Mott BT, Shrimp JH, Moses MA, Lee M-J, Yuno A, Lee TD, Hu X, Anderson T, Kusewitt D, Hathaway HH, Jadhav A, Picard D, Trepel JB, Mitchell JB, Stott GM, Moore W, Simeonov A, Sklar LA, Norenberg JP, Linehan WM, Maloney DJ, Dang CV, Waterson AG, Hall M, Darley-Usmar VM, Krishna MC, Neckers LM. *Cell Rep.* **2020** Feb 11;30(6):1798-1810.e4. doi: 10.1016/j.celrep.2020.01.039.

#### **Targeting Glycolysis Through Inhibition of Lactate Dehydrogenase Impairs Tumor Growth in Preclinical Models of Ewing Sarcoma.**

Yeung C, Gibson AE, Issaq SH, Oshima N, Baumgart JT, Edessa LD, Rai G, Urban DJ, Johnson MS, Benavides GA, Squadrito GL, Yohe ME, Lei H, Eldridge S, Hamre J 3rd, Dowdy T, Ruiz-Rodado V, Lita A, Mendoza A, Shern JF, Larion M, Helman LJ, Stott GM, Krishna MC, Hall MD, Darley-Usmar V, Neckers LM, Heske CM. *Cancer Res.* **2019**;79(19):5060-5073.

#### **Thiazole Derivatives as Inhibitors for the Treatment of Cancer Cells Resistant.**

Robert B. Kargbo RB. *ACS Med Chem Lett.* **2018**;9(3):169–170. doi: 10.1021/acsmedchemlett.8b00069.

#### **Discovery and Optimization of Potent, Cell-Active Pyrazole-Based Inhibitors of Lactate Dehydrogenase (LDH).**

Rai G, Brimacombe KR, Mott BT, Urban DJ, Hu X, Yang S-M, Lee TD, Cheff DM, Kouznetsova J, Benavides GA, Pohida K, Kuenstner EJ, Luci DK, Lukacs CM, Davies DR, Dranow DM, Zhu H, Sulikowski G, Moore WJ, Stott GM, Flint AJ, Hall MD, Darley-Usmar VM, Neckers LM, Dang CV, Waterson AG, Simeonov A, Jadhav A, Maloney DJ. *J Med Chem.* **2017**;60(22):9184–9204.

### **Patents:**

1 h-pyrazol-1-yl-thiazoles as inhibitors of lactate dehydrogenase and methods of use thereof, WO 2018005807 A1, PCT Int. Appl. (2018), WO 2018005807 A1.

Small molecule inhibitors of lactate dehydrogenase and methods of use thereof, WO 2016109559 A3 PCT Int. Appl. (2016), WO 2016109559 A2.

## **Mcl-1:**

### **Discovery of Potent Myeloid Cell Leukemia-1 (Mcl-1) Inhibitors That Demonstrate in Vivo Activity in Mouse Xenograft Models of Human Cancer.**

Lee T, Christov PP, Shaw S, Tarr JC, Zhao B, Veerasamy N, Jeon KO, Mills JJ, Bian Z, Sensintaffar JL, Arnold AL, Fogarty SA, Perry E, Ramsey HE, Cook RS, Hollingshead M, Davis Millin M, Lee KM, Koss B, Budhraj A, Opferman JT, Kim K, Arteaga CL, Moore WJ, Olejniczak ET, Savona MR, Fesik SW. *J Med Chem.* **2019**;62(8):3971-3988.

### **A novel MCL1 inhibitor combined with venetoclax rescues venetoclax-resistant acute myelogenous leukemia.**

Ramsey HE, Fischer MA, Lee T, Gorska AE, Arrate MP, Fuller L, Boyd KL, Strickland SA, Sensintaffar JL, Hogdal LJ, Ayers GD, Olejniczak ET, Fesik SW, Savona MR. *Cancer Discovery* **2018**; 8:1566-1581.

### **Understanding the Species Selectivity of Myeloid Cell Leukemia-1 (Mcl-1) Inhibitors.**

Zhao B, Arnold AL, Coronel MA, Lee JH, Lee T, Olejniczak ET, Fesik SW. *Biochemistry.* **2018**;57(32):4952-4958.

### **Optimization of Potent and Selective Tricyclic Indole Diazepinone Myeloid Cell Leukemia-1 (Mcl-1) Inhibitors Using Structure-Based Design.**

Shaw S, Bian Z, Zhao B, Tarr JC, Veerasamy N, Jeon KO, Belmar J, Arnold AL, Fogarty SA, Perry E, Sensintaffar JL, Camper DV, Rossanese OW, Lee T, Olejniczak ET, Fesik SW. *J Med Chem.* **2018**;61(6): 2410-21.

### **MYC and MCL1 Cooperatively Promote Chemotherapy-Resistant Breast Cancer Stem Cells via Regulation of Mitochondrial Oxidative Phosphorylation.**

Lee K-m, Giltneane JM, Balko JM, Schwarz LJ, Guerrero-Zotano AL, Hutchinson KE, Nixon MJ, Estrada MV, Sanchez V, Sanders ME, Lee T, Gomez H, Lluch A, Perez-Fidalgo JA, Wolf MM, Andrejeva G, Rathmell JC, Fesik SW, Arteaga CL. *Cell Metabolism* **2017**; 26:633–647.

### **Structure of a Myeloid cell leukemia-1 (Mcl-1) inhibitor bound to drug site 3 of Human Serum Albumin.**

Zhao B, Sensintaffar J, Bian Z, Belmar J, Lee T, Olejniczak ET, Fesik SW. *Bioorganic & Medicinal Chemistry.* **2017**;25(12):3087-3092.

### **Discovery and biological characterization of potent myeloid cell leukemia-1 inhibitors.**

Lee T, Bian Z, Zhao B, Hogdal LJ, Sensintaffar JL, Goodwin CM, Belmar J, Shaw S, Tarr JC, Veerasamy N, Matulis SM, Koss B, Fischer MA, Arnold AL, Camper DV, Browning CF, Rossanese OW, Budhraj A, Opferman J, Boise LH, Savona MR, Letai A, Olejniczak ET, Fesik SW. *FEBS Lett.* **2017**;591(1):240–251.

### **Discovery of 2-Indole-acylsulfonamide myeloid cell leukemia 1 (Mcl-1) inhibitors using fragment-based methods.**

Pelz NF, Bian Z, Zhao B, Shaw S, Tarr JC, Belmar J, Gregg C, Camper DV, Goodwin CM, Arnold AL, Sensintaffar JL, Friberg A, Rossanese OW, Lee T, Olejniczak ET, Fesik SW. *J Med Chem.* **2016**;59(5):2054-2066.

### **Small molecule Mcl-1 inhibitors for the treatment of cancer.**

Belmar J, Fesik SW. *Pharmacol Ther.* **2015**;145:76-84.

### **Myeloid cell leukemia-1 is an important apoptotic survival factor in triple-negative breast cancer.**

Goodwin CM, Rossanese OW, Olejniczak ET, Fesik SW. *Cell Death & Differentiation* **2015**;22:2098-2106.

### **Discovery of tricyclic indoles that potently inhibit Mcl-1 using fragment-based methods and structure-based design.**

Burke JP, Bian Z, Shaw S, Zhao B, Goodwin CM, Belmar J, Browning CF, Vigil D, Friberg A, Camper DV, Rossanese OW, Lee T, Olejniczak ET, Fesik SW. *J Med Chem.* **2015**;58(9):3794-3805.

### **Discovery of potent myeloid cell leukemia 1 (Mcl-1) inhibitors using fragment-based methods and structure-based design.**

Friberg A, Vigil D, Bin Z, Daniels RN, Burke JP, Garcia-Barrantes PM, Camper D, Chauder BA, Lee T, Olejniczak ET, Fesik SW. *J Med Chem.* **2013**;56(1):15–30.

## **Patents:**

Lee T, Tarr JC, Jeon K, Salovich JM, Shaw S, Veerasamy N, Kim K, Christov PP, Olejniczak ET, Zhao B, Fesik SW. Substituted indoles as Mcl-1 inhibitors and their preparation. PCT Int. Appl. WO 2017152076 A1 20170908. **2017**.

Lee T, Burke JP, Olejniczak ET, Belmar J, Bian Z, Fesik SW. Tricyclic Indole Mcl-1 Inhibitors as antitumor agents. U.S. Pat. Appl. US 20160106731 A1 20160421. **2016**.

Lee T, Bian Z, Belmar J, Christov PP, Pelz NF, Shaw S, Kim K, Tarr JC, Olejniczak ET, Zhao B, Fesik SW. Substituted indoles Mcl-1 inhibitors and their preparation. PCT Int. Appl. WO 2015148854 A1 20151001. **2015**.

Lee T, Kim K, Christov PP, Belmar J, Burke JP, Olejniczak ET, Fesik SW. Substituted indole Mcl-1 inhibitors. PCT Int. Appl. WO 2015031608 A1 20150305. **2015**.

Lee T, Pelz NF, Belmar J, Bian Z, Olejniczak ET, Fesik SW, Chauder BA. Preparation of substituted benzofurans, benzothiophenes and indoles as selective Mcl-1 inhibitors. PCT Int. Appl. WO2014047427 A2 20140327. **2014**.

Lee T, Pelz NF, Belmar J, Bian Z, Olejniczak ET, Fesik SW, Chauder BA. Preparation of substituted benzofurans, benzothiophenes and indoles as selective Mcl-1 inhibitors. PCT Int. Appl. WO2014047427 A2. **2013**.

## **Mer Kinase:**

### **UNC2025, a potent and orally bioavailable MER/FLT3 dual inhibitor.**

Zhang W, DeRyckere D, Hunter D, Liu J, Stashko M, Minson KA, Cummings CT, Lee M, Glaros TG, Newton DL, Sather S, Zhang D, Kireev D, Janzen WP, Earp HS, Graham DK, Frye SV, Wang X. *J Med Chem.* **2014**;57(16):7031–7041.

### **UNC1062, a new and potent Mer inhibitor.**

Liu J, Zhang W, Stashko MA, DeRyckere D, Cummings CT, Hunter D, Yang C, Jayakody CN, Cheng N, Simpson C, Norris-Drouin J, Sather S, Kireev D, Janzen WP, Earp HS, Graham DK, Frye SV, Wang X. *Eur J Med Chem.* **2013**;65:83–93.

### **MERTK receptor tyrosine kinase is a therapeutic target in melanoma.**

Schlegel J, Sambade MJ, Sather S, Moschos SJ, Tan AC, Wings A, Deryckere D, Carson CC, Trembath DG, Tentler JJ, Eckhardt SG, Kuan PF, Hamilton RL, Duncan LM, Miller CR, Nikolaishvili-Feinberg N, Midkiff BR, Liu J, Zhang W, Yang C, Wang X, Frye SV, Earp HS, Shields JM, Graham DK. *J Clin Invest* **2013**;123(5):2257–2267.

### **UNC569, a novel small-molecule Mer inhibitor with efficacy against acute lymphoblastic leukemia in vitro and in vivo.**

Christoph S, DeRyckere D, Schlegel J, Frazer JK, Batchelor LA, Trakhimets AY, Sather S, Hunter DM, Cummings CT, Liu J, Yang C, Kireev D, Simpson C, Norris-Drouin J, Hull-Ryde EA, Janzen WP, Johnson GL, Wang X, Frye SV, Earp HS, Graham DK. *Mol Cancer Ther.* **2013**;12:2367–2377.

### **Discovery of Mer specific tyrosine kinase inhibitors for the treatment and prevention of thrombosis.**

Zhang W, McIver A L, Stashko M A, Deryckere D, Branchford BR, Hunter D, Kireev D, Miley MJ, Norris-Drouin, J, Stewart WM, Lee M, Sather S, Zhou Y, Di Paola JA, Machius M, Janzen WP, Earp HS, Graham DK, Frye SV, Wang X. *J Med Chem.* **2013**;56: 9693–9700.

### **Pseudo-cyclization through intramolecular hydrogen bond enables discovery of pyridine substituted pyrimidines as new Mer kinase inhibitors.**

Zhang W, Zhang D, Stashko MA, Deryckere D, Hunter D, Kireev D, Miley MJ, Cummings C, Lee M, Norris-Drouin J, Stewart WM, Sather S, Zhou Y, Kirkpatrick G, Machius M, Janzen WP, Earp HS, Graham DK, Frye SV, Wang X. *J Med Chem.* **2013**;56:9683–9692.

### **Efficient solution-phase synthesis of 4,5,7-trisubstituted pyrrolo[3,2-d]pyrimidines.**

Zhang W, Liu J, Stashko MA, Wang X. *ACS. Comb. Sci.* **2013**;15(1):10–19.

### **Discovery of small molecule Mer kinase inhibitors for the treatment of pediatric acute lympho- blastic leukemia.**

Liu J, Yang C, Simpson C, DeRyckere D, Van DA, Miley MJ, Kireev D, Norris-Drouin J, Sather S, Hunter D, Korboukh VK, Patel HS, Janzen WP, Machius M, Johnson GL, Earp HS, Graham DK, Frye SV, Wang X. *ACS Med Chem Lett.* **2012**;3:129–134.

## **Patents:**

Wang X, Liu J, Yang C, Zhang W, Frye S, Kireev D. Preparation of pyrazolopyrimidine compounds as Mer inhibitors for the treatment of cancer and inhibition of blood clot formation. PCT Int. Appl. WO2014062774 A1. **2013**.

Wang X, Zhang W, Frye SV, Kireev D, McIver AL, Liu J. Pyrimidine compounds for the treatment of cancer. PCT/US2013/071409. **2013**.

Wang X, Zhang W, Kireev D, Zhang D, McIver A. Pyrimidine compounds for the treatment of cancer. PCT/US13/42033, WO2013177168 A1 20131128. **2013**.

Wang X, Liu J, Zhang W, Frye S, Kireev D. Pyrrolopyrimidine compounds for the treatment of cancer. PCT/US2012/058298, WO2013/052417 A1, US2013/641,729. **2012**.



Wang X, Liu J, Yang C, Zhang W, Frye S, Kireev D. Pyrazolopyrimidine compounds for the treatment of cancer. PCT/US2011/036215, WO2011146313 A1, US2012/61714841. **2011**.

## **NNMT:**

### **Proteomics reveals NNMT as a master metabolic regulator of cancer-associated fibroblasts.**

Eckert MA, Coscia F, Chryplewicz A, Chang JW, Hernandez KM, Pan S, Tienda SM, Nahotko DA, Li G, Blaženović I, Lastra RR, Curtis M, Yamada SD, Perets R, McGregor SM, Andrade J, Fiehn O, Moellering RE, Mann M, Lengyel E. *Nature*. **2019**;569(7758):723-728.

## **SHP2:**

### **Discovery of novel furanylbenzamide inhibitors that target oncogenic tyrosine phosphatase SHP2 in leukemia cells.**

Raveendra-Panickar D, Finlay D, Layng FI, Lambert L, Celeridad M, Zhao M, Barbosa K, De Backer LJS, Kwong E, Gosalia P, Rodiles S, Holleran J, Ardecky R, Grotegut S, Olson S, Hutchinson JH, Pasquale EB, Vuori K, Deshpande AJ, Cosford NDP, Tautz L. *J Biol Chem*. **2022** Jan; 298(1):101477. doi: 10.1016/j.jbc.2021.101477. Online ahead of print.

### **A cellular target engagement assay for the characterization of SHP2 (PTPN11) phosphatase inhibitors.**

Romero C, Lambert LJ, Sheffler DJ, De Backer LJ, Raveendra-Panickar D, Celeridad M, Grotegut S, Rodiles S, Holleran J, Sergienko E, Pasquale EB, Cosford NDP, Tautz L. *J Biol Chem*. **2020** Feb 28; 295(9):2601-2613. doi: 10.1074/jbc.RA119.010838. Epub 2020 Jan 17.

## **STAT3:**

### **High Content Imaging Assays for IL-6-Induced STAT3 Pathway Activation in Head and Neck Cancer Cell Lines.**

Johnston PA, Sen M, Hua Y, Camarco DP, Shun TY, Lazo JS Grandis JR.. *Methods Mol Biol*. **2018**;1683:229-244.

### **Mechanism of action of selective inhibitors of IL-6 induced STAT3 pathway in head and neck cancer cell lines.**

Sen M, Johnston PA, Pollock NI, DeGrave K, Joyce SC, Freilino ML, Hua Y Camarco DP, Close DA, Huryn DM, Wipf P, Grandis JR. *J Chem Biol*. **2017**;10(3):129-141.

### **Toxicity, pharmacokinetics and metabolism of a novel inhibitor of IL-6-induced STAT3 activation.**

Kiesel BF, Parise RA, Guo J, Huryn DM, Johnston PA, Colombo R, Sen M, Grandis JR, Beumer JH, Eiseman JL. *Cancer Chemother Pharmacol*. **2016**;78(6):1225-1235.

### **Optimization of pyrazole-containing 1,2,4-triazolo-[3,4-b]thiadiazines, a new class of STAT3 pathway inhibitors.**

LaPorte MG, Wang Z, Colombo R, Garzan A, Peshkov VA, Liang M, Johnston PA, Schurdak ME, Sen M, Camarco DP, Hua Y, Pollock NI, Lazo JS, Grandis JR, Wipf P, Huryn DM. *Bioorg Med Chem Lett*. **2016**;26(15):3581-3585.

### **A metric and workflow for quality control in the analysis of heterogeneity in phenotypic profiles and screens.**

Gough A, Shun T, Taylor DL, Schurdak M. *Methods*. **2016**;96:12-26.

### **HCS campaign to identify selective inhibitors of IL-6-induced STAT3 pathway activation in head and neck cancer cell lines.**

Johnston PA, Sen M, Hua Y, Camarco DP, Shun TY, Lazo JS, Wilson GM, Resnick LO, LaPorte MG, Wipf P, Huryn DM, Grandis JR. *Assay Drug Dev Technol*. **2015**;13:356-76.

### **High-content pSTAT3/1 imaging assays to screen for selective inhibitors of STAT3 pathway activation in head and neck cancer cell lines.**

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