

NExT Discovery Project Publications

AAA ATPase p97:

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

James C. Burnett, Chaemin Lim, Brian D. Peyser, Lalith P. Samankumara, Marina Kovaliov, Raffaele Colombo, Stacie L. Bulfer, Matthew G. LaPorte, Ann R. Hermone, Connor F. McGrath, Michelle R. Arkin, Rick Gussio, Donna M. Huryn & Peter Wipf, *Org. Biomol. Chem.* **2017**, 15, 4096

Structure–Activity Study of Bioisosteric Trifluoromethyl and Pentafluorosulfanyl Indole Inhibitors of the AAA ATPase p97

Celeste Alvarez, Michelle R. Arkin, Stacie L. Bulfer, Raffaele Colombo, Marina Kovaliov, Matthew G. LaPorte, Chaemin Lim, Mary Liang, William J. Moore, R. Jeffrey Neitz, Yongzhao Yan, Zhizhou Yue, Donna M. Huryn & Peter Wipf, *ACS Med Chem. Lett.* **2015**, 6, 1225-30

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

Fang, C.J., Gui, L., Zhang, X., Moen, D.R., Li, K., Frankowski, K.J., Lin, H. J., Schoenen, F.J. & Chou, T.-F., *ChemMedChem.* **2015**, 10, 52-56

Altered cofactor regulation with disease-associated p97/VCP mutations

Zhang, X., Gui, L., Zhang, X., Bulfer, S.L., Sanghez, V., Wong, D.E., Lee, Y., Lehmann, L., Lee, J.S., Shih, P.Y., Lin, H.J., Iacovino, M., Wehl, C.C., Arkin, M.R., Wang, Y. & Chou, T.F., *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, M.S., Bulfer, S.L., Neitz, R.J., Renslo, A.R., Jacobson, M.P., James, T.L., Arkin, M.R. & Kelly, M.J., *J Biomol Screen.* **2015**, 20, 788-800

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

Chou, T.-F., Bulfer, S. L., Wehl, C.C., Li, K., Lis, L.G., Walters, M.A., Schoenen, F.J., Lin, H.J., Deshaies, R.J. & Arkin, M.R., *J. Mol. Biol.* **2014**, 426, 2886–2899

Structure–activity relationship study reveals ML240 and ML241 as potent and selective inhibitors of p97 ATPase

Chou, T.-F., Li, K., Frankowski, K.J., Schoenen, F.J. & Deshaies, R.J., *ChemMedChem*, **2013**, 8, 297–312

Mcl-1:

Discovery of Tricyclic Indoles That Potently Inhibit Mcl-1 Using Fragment-Based Methods and Structure-Based Design

Burke, J.P., Bian, Z., Shaw, S., Zhao, B., Goodwin, C.M., Belmar, J., Browning, C.F., Vigil, D., Friberg, A., Camper, D.V., Rossanese, O.W., Lee, T., Olejniczak, E.T. & Fesik, S.W., *J Med Chem.* **2015**, 58, 3794-805

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Small molecule Mcl-1 inhibitors for the treatment of cancer

Belmar, J. & Fesik, S.W., *Pharmacol Ther.* **2015**, *145*, 76-84

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, R.N., Burke, J.P., Garcia-Barrantes, P.M., Camper, D., Chauder, B.A., Lee, T., Olejniczak, E.T. & Fesik, S.W., *J. Med. Chem.* **2013**, *56*, 15–30

WDR5-MLL1:

Interaction with WDR5 promotes target gene recognition and tumorigenesis by MYC

Thomas L.R., Wang Q., Grieb B.C., Phan J., Foshage A.M., Sun Q., Olejniczak E.T., Clark T., Dey S., Lorey S., Alcie B., Howard G.C., Cawthon B., Ess K.C., Eischen C.M., Zhao Z., Fesik S.W. & Tansey W.P., *Mol Cell.* **2015**, *58*, 440-52

Mer Kinase:

UNC2025, A potent and orally bioavailable MER/FLT3 dual inhibitor

Zhang, W., DeRyckere, D., Hunter, D., Liu, J., Stashko, M., Minson, K.A., Cummings, C.T., Lee, M., Glaros, T.G., Newton, D.L., Sather, S., Zhang, D., Kireev, D., Janzen, W.P., Earp, H.S., Graham, D.K., Frye, S.V. & Wang, X., *J. Med. Chem.* **2014**, *57*, 7031–7041

UNC1062, a new and potent Mer inhibitor

Liu, J., Zhang, W., Stashko, M.A., DeRyckere, D., Cummings, C.T., Hunter, D., Yang, C., Jayakody, C.N., Cheng, N., Simpson, C., Norris-Drouin, J., Sather, S., Kireev, D., Janzen, W.P., Earp, H.S., Graham, D.K., Frye, S.V. & Wang, X., *Eur. J. Med. Chem.* **2013**, *65*, 83–93

MERTK receptor tyrosine kinase is a therapeutic target in melanoma

Schlegel, J., Sambade, M.J., Sather, S., Moschos, S.J., Tan, A.C., Wings, A., Deryckere, D., Carson, C.C., Trembath, D.G., Tentler, J.J., Eckhardt, S.G., Kuan, P.F., Hamilton, R.L., Duncan, L.M., Miller, C.R., Nikolaishvili-Feinberg, N., Midkiff, B.R., Liu, J., Zhang, W., Yang, C., Wang, X., Frye, S.V., Earp, H.S., Shields, J.M. & Graham, D.K., *J. Clin. Invest.* **2013**, *123*, 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, J.K., Batchelor, L.A., Trakhimets, A.Y., Sather, S., Hunter, D.M., Cummings, C.T., Liu, J., Yang, C., Kireev, D., Simpson, C., Norris-Drouin, J., Hull-Ryde, E.A., Janzen, W.P., Johnson, G.L., Wang, X., Frye, S.V., Earp III, H.S. & Graham, D.K., *Mol. Cancer Ther.* **2013**, *12*, 2367–2377

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

Zhang, W., Zhang, D., Stashko, M.A., Deryckere, D., Hunter, D., Kireev, D., Miley, M.J., Cummings, C., Lee, M., Norris-Drouin, J., Stewart, W.M., Sather, S., Zhou, Y., Kirkpatrick, G., Machius, M., Janzen, W.P., Earp, H.S., Graham, D.K., Frye, S.V. & Wang, X., *J. Med. Chem.* **2013**, *56*, 9683–9692

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, D.A., Miley, M.J., Kireev, D., Norris-Drouin, J., Sather, S., Hunter, D., Korboukh, V.K., Patel, H.S., Janzen, W.P., Machius, M., Johnson, G.L., Earp, H.S., Graham, D.K., Frye, S.V. & Wang, X., *ACS Med. Chem. Lett.* **2012**, *3*, 129–134

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

Zhang, W., Liu, J., Stashko, M.A. & Wang, X., *ACS. Comb. Sci.* **2012**, *15*, 10–19

STAT3:

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

Albert Gough, Tong Ying Shun, D. Lansing Taylor, Mark Schurdak, *Methods* [Online Early Access]. DOI: 10.1016/j.ymeth.2015.10.007 (accepted manuscript, has not undergone final copyediting, typesetting, or proof review)

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

Johnston, P.A., Sen, M., Hua, Y., Camarco, D.P., Shun, T.Y., Lazo, J.S., Wilson, G.M., Resnick, L.O., LaPorte, M.G., Wipf, P., Huryn, D.M. & Grandis, J.R., *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

Johnston, P.A., Sen, M., Hua, Y., Camarco, D., Shun, T.Y., Lazo, J.S. & Grandis, J.R., *Assay Drug Dev. Technol.* **2014**, *12*, 55–79

2-Guanidinoquinazolines as new inhibitors of the STAT3 pathway

LaPorte, M.G., Paz Lima, D.J., Zheng, F., Sen, M., Grandis, J.R., Camarco, D., Hua, Y., Johnston, P.A., Lazo, J.S., Resnick, L.O., Wipf, P. & Huryn, D. M., *Bioorg. Med. Chem. Lett.* **2014**, *24*, 5081–85

STAT3 signaling: anticancer strategies and challenges

Johnston, P.A. & Grandis, J.R., *Mol. Interv.* **2011**, *11*, 18–26

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Artemis Endonuclease:

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

Li, S., Chang, H.H., Niewolik, D., Hedrick, M.P., Pinkerton, A.B., Hassig, C.A., Schwarz, K. & Lieber, MR., *J. Biol. Chem.* **2014**, 289, 7825-34

Natural Product Inducers of Apoptosis:

Ultra high throughput screening of natural product extracts to identify pro-apoptotic inhibitors of BCL-2 family proteins

Hassig, C.A., Zeng, F.Y., Kung, P., Kiankarimi, M., Kim, S., Diaz, P.W., Zhai, D., Welsh, K., Morshedian, S., Su, Y., O'Keefe, B., Newman, D.J., Rusman, Y., Kaur, H., Salomon, C. E., Brown, S.G., Baire, B., Michel, A.R., Hoye, T.R., Francis, S., Georg, G.I., Walters, M.A., Divlianska, D.B., Roth, G.P., Wright, A.E. & Reed, J. C., *J. Biomol. Screen*, **2014**, 19, 1201–1211

T-dCyd:

Novel DNA methyltransferase-1 (DNMT1) depleting anticancer nucleosides, 4'-thio-2'-deoxycytidine and 5-aza-4'-thio-2'-deoxycytidine

Jaideep V. Thottassery, Vijaya Sambandam, Paula W. Allan, Joseph A. Maddry, Yulia Y. Maxuitenko, Kamal Tiwari, Melinda Hollingshead, William B. Parker, *Cancer Chemother Pharmacol.* **2014**, 74, 291-302

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, 1030-40

Histone Demethylases:

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

Horton, J.R., Engstrom, A., Zoeller, E.L., Liu, X., Shanks, J.R., Zhang, X., Johns, M.A., Vertino, P.M., Fu, H., Cheng, X., *J Biol. Chem.* [Online Early Access]. DOI: 10.1074/jbc.M115.698449

IDH1:

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, Karavadhi S, Shah P, Lee OW, Wang A, Mclver A, Zheng H, Wang X, Xu X, Jadhav A, Simeonov A, Shen M, Boxer MB, Hall MD., *Sci Rep.* **2017** Oct 6;7(1):12758. doi: 10.1038/s41598-017-12630-x