CURRICULUM VITAE

Xiangshu Xiao, Ph.D.

Professor
Department of Chemical Physiology and Biochemistry
Knight Cancer Institute
Oregon Health & Science University
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Professional Experience

July 2019-present Professor (with tenure) Department of Chemical Physiology and Biochemistry, Oregon Health & Science University, Portland, OR

July 2018-June 2019 Professor (with tenure) Program in Chemical Biology, Department of Physiology and Pharmacology, Oregon Health & Science University, Portland, OR

July 2014-June 2018 Associate Professor Program in Chemical Biology, Department of Physiology and Pharmacology, Oregon Health & Science University, Portland, OR

Dec 2007-present Member, Knight Cancer Institute, Oregon Health & Science University, Portland, OR

Aug. 2007-June 2014 Assistant Professor Program in Chemical Biology, Department of Physiology and Pharmacology, Oregon Health & Science University, Portland, OR

Jul. 2005-Jul. 2007 Post-doctoral Fellow, Chemical Biology, University of Texas Southwestern Medical Center, Dallas, Texas
Advisor: Prof. Thomas Kodadek
Research Focus: Development of Artificial Transcription Activators.

Education

Aug. 2001-Jun. 2005 Ph.D., Medicinal Chemistry, Purdue University, West Lafayette, Indiana
Advisor: Prof. Mark Cushman
Dissertation: Chemistry and Biology of Topoisomerase I Inhibitors: Indenoisoquinolines and Camptothecins.

Sep. 1998-Jun. 2001 M.Sc., Organic Chemistry, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, China
Advisor: Prof. Donglu Bai
Thesis: Studies on the Total Synthesis of Macrolactin A and its Analogs

Sep. 1994-Jun. 1998 B.Sc., Medicinal Chemistry, Beijing Medical University, Beijing, China
Advisor: Prof. Lihe Zhang
Thesis: Synthesis of Isonucleosides.

Award

1995-1997 Excellent Student Scholarship, Beijing Medical University.
1998 Excellent Undergraduate Research Thesis.
2001 Yongling Liu Scholarship, Shanghai Institute of Materia Medica, Chinease Academy of Sciences
2004 Outstanding Research Thesis, Shanghai
2005 Travel Grant Award, Division of Medicinal Chemistry, American Chemical Society.
2006 Sigma Xi Postdoctoral Research Competition Award (UT Southwestern)
2009 OHSU Top Technology Innovation Award
2010 Oregon BIRCWH Scholar (declined due to concurrent R01 funding)
2014 OHSU Technology Transfer and Business Development Award
2016 Best Poster Award, Gordon Research Conference on Intermediate Filaments
2016 OHSU Technology Transfer and Business Development Award

Open source contribution

The Xiao laboratory believes an open-source research model. We have developed many small molecule tools that become widely available free of strings from different commercial sources including Tocris, Calbiochem (EMD Millipore), MedChem Express and Glixx Laboratories. The following unique chemicals were originated from our lab: **666-15** (CREB), **653-47** (CREB), **LBL1** (lamin).

Publications (* denotes corresponding author)

1. Alkayed, N. J.;* Cao, Z.; Qian, Z.; Nagarajan, S.; Liu, X.; Nelson, J.; Xie, F.; Li, B. X.; Fan, W.; Liu, L.; Grafe, M. R.; **Xiao, X**.;* Barnes, A. P.;* Kaul, S.* "Bidirectional Control of Coronary Vascular Resistance by Eicosanoids via a Novel GPCR", bioRxiv, DOI: 10.1101/420406. (*co-senior authors)
2. Li, B. X.; **Xiao, X.*** "A suite of bioassays to evaluate CREB inhibitors" *Methods in Enzymology* **2020**, doi.org/10.1016/bs.mie.2019.11.002.
3. Xie, F.; Fan, Q.; Li, B. X.*; **Xiao, X.*** "Discovery of a Synergistic Inhibitor of cAMP-Response Element Binding Protein (CREB)-mediated Gene Transcription with 666-15" *J. Med. Chem.*, **2019**, *62*, 11423-11429.

4. Brown, P.; **Xiao, X.** (part of RELISH Consortium with >1000 authors); Zhou, Y.* "Large expert-curated database for benchmarking document similarity detection in biomedical literature search" *Database*, **2019**, 1-66, doi.org/10.1093/database/baz085.
5. **Xiao, X.**; Li, B. X.* "Identification of Lamins as the Molecular Targets of LBL1 using a clickable photoaffinity probe" *Methods in Enzymology***, 2019**, doi.org/10.1016/bs.mie.2019.02.038.
6. Jiang, M.; Yan, Y.; Yang, Kai, Liu, Z.; Qi, J.; Zhou, H.; Qian, N.; Zhou, Q.; Wang, F.; Wang, T.; Xu, X.; **Xiao, X.**; Deng, L. "Small molecule nAS-E targeting cAMP response element binding protein (CREB) and CREB-binding protein interaction inhibits breast cancer bone metastasis", *J. Cell. Mol. Med.*, **2019**, 23, 1224-1234.
7. Duque-Afonso, J. Lin, C. H. Han, K. Morgens, D. W. Jeng, E. E. Weng, Z. Jeong, J. Wong, S. H. K. Zhu, L. Wei, M. C. Chae, H. D. Schrappe, M. Cario, G. Duyster, J. **Xiao, X.** Sakamoto, K. M. Bassik, M. C. Cleary, M. L. "CBP modulates sensitivity to dasatinib in pre-BCR+ acute lymphoblastic leukemia" *Cancer Res.*, **2018**, *78*, 6497-6508.
8. Li, B. X.;* Chen, J.; Chao, B.; Zheng, Y.; **Xiao, X.*** "A Lamin-Binding Ligand Inhibits Homologous Recombination Repair of DNA Double-Strand Breaks" *ACS Cent. Sci.* **2018**, *4*, 1201-1210.
9. Li, B. X.;* Chen, J.; Chao, B.; David, L; **Xiao, X.*** "A lamin-binding ligand LBL1 targets nuclear lamins, *ACS Chem. Biol.,* **2018**, *13*, 1380-1387.
10. Sanford-Crane, H.; Pejovic, T.; **Xiao, X.*** "Drugging Homologous Recombination: Back to the Future" *Future Medicinal Chemistry*, **2018**, *10*, 1279-1281.
11. Meng, Q.; Li, B. X.; **Xiao, X.*** "Towards Developing Chemical Modulators of Hsp60 as Potential Therapeutics" *Front. Mol. Biosci.,* **2018**, doi: 10.3389/fmolb.2018.00035.
12. Chao, B.; Li, B. X. **Xiao, X.*** "Design, synthesis and evaluation of antitumor acylated monoaminopyrroloquinazolines" *Bioorg. Med. Chem. Lett.*, **2017**, *27*, 3107-3110.
13. Liu, X.; Qian, Z.; Cao, Z.; Xie, F.; Fan, W.; **Xiao**, **X.**; Barnes, A. P.; Kaul, S.; Alkayed, N. J.* "Functional Screening for G Protein-coupled Receptor Targets of 14,15-Epoxyeicosatrienoic Acid" *Prostaglandins and Other Lipid Mediators*, **2017**, *132*, 31-40.
14. Xie, F.; Li, B. X.; **Xiao, X.*** "Design, Synthesis and Biological Evaluation of Regioisomers of 666-15 as Inhibitors of CREB-mediated Gene Transcription" *Bioorg. Med. Chem. Lett.*, **2017**, *27,* 994-998.
15. Li, B. X.; Gardner, R.; Xue, C.; Qian, D. Z.; Xie, F.; Thomas, G.; Kazmierczak, S. C.; Habecker, B. A.; **Xiao, X.*** "Systemic Inhibition of CREB is Well-tolerated in vivo" *Scientific Reports*, **2016**, 6, 34513.
16. Francois, S.; Sen, N.; Mitton, B.; **Xiao, X.**, Sakamoto, K.; Arvin, A.* "Varicella-Zoster virus activates CREB and Inhibition of the pCREB-p300/CBP-interaction inhibits viral replicaiton in vitro and skin pathogenesis in vivo" *J. Virol.*, **2016**, *90*, 8686-8697.

17. Mitton, B.; Chae, H-D; Hsu, K.; Dutta, R.; Aldana-Masangkay, G.; Ferrari, R.; Davis, K.; Tiu, B.; Kaul, A.; Lacayo, N.; Dahl, G.; Xie, F.; Li, B.; Breese, M.; Landaw, E.; Nolan, G.; Pellegrini, M.; Romanov, S.; **Xiao, X.**; Sakamoto, K.* "Small Molecule Inhibition of cAMP Response Element Binding Protein in Human Acute Myeloid Leukemia Cells" *Leukemia*, **2016**, *30*, 2302-2311.
18. Xie, F.; Li, B. X.; Kassenbrock, A.; Xue, C.; Wang, X.; Qian, D. Z.; Sears, R. C.; **Xiao, X.*** "Identification of a Potent Inhibitor of CREB-Mediated Gene Transcription with Efficacious in Vivo Anticancer Activity" *J. Med. Chem.*, **2015**, *58,* 5075–5087. (Highlighted in *Biocentury Innovations* (formerly *SciBX*), *Labbase News*) (We made this inhibitor available free of strings from Tocris, Calbiochem (EMD Millipore) and MedChem Express)
19. Kang, X.; Lu, Z.; Cui, C.; Fan, Y.; Dong, B.; Han, X.; Xie, X.; Tyner, J. W.; Coligan, J. E.; Collins, R. H.; **Xiao, X.**; You, J. M.; Zhang, C. C.* "The ITIM-containing receptor LAIR1 is essential for acute myeloid leukemia development" *Nat. Cell Biol.*, **2015**, 17, 665-677 (Highlighted in *UT Southwestern News*, *ScienceDaily*, *MedicalXpress*, *Bionews-TX*, *Biocentury Innovations (formerly SciBX)* and *BioQuick News*).
20. Chao, B.; Li, B. X.; **Xiao, X.*** "The chemistry and pharmacology of privileged pyrroloquinazolines" *MedChemComm*, **2015**, 6, 510-520.
21. Xie, F.; Li, B. X.; Alkayed, N. J.; **Xiao, X.*** "Synthesis of 14,15-EET from Arachidonic Acid Using Urea-Hydrogen Peroxide as the Oxidant" *Synthetic Commun.*, **2015**, *45*, 105-110.
22. Li, B. X.; Xie, F.; Fan, Q.; Barnhart, K. M.; Moore, C. E.; Rheingold, A. L.; **Xiao, X.*** "Novel Type of Prodrug Activation through a Long-range *O,N*-Acyl Transfer: a Case of Water-Soluble CREB Inhibitor " *ACS Med. Chem. Lett.*, **2014**, *5*, 1104-1109.
23. Xie, F.; Li, B. X.; Broussard, C.; **Xiao, X.*** "Identification, Synthesis and Evaluation of Substituted Benzofurazans as Inhibitors of CREB-mediated Gene Transcription" *Bioorg. Med. Chem. Lett.* **2013**, *23*, 5371-5375.
24. Chen, J.; Kassenbrock, A.; Li, B. X.; **Xiao, X.*** "Discovery of a Potent Anti-tumor Agent through Regioselective Mono-*N*-acylation of 7*H*-Pyrrolo[3,2-*f*]quinazoline-1,3-diamine" *MedChemComm, ,* **2013**, *4*, 1275-1282.
25. Xie, F.; Li, B. X.; **Xiao, X.*** "Synthesis and Evaluation of an *O*-Aminated Naphthol AS-E as a Prodrug of CREB-mediated Gene Transcription Inhibition" *Lett. Org. Chem.,* **2013**, *10*, 380-384.
26. Nelson, J. W.; Subrahmanyan, R. M.; Summers, S. A.; **Xiao, X.**; Alkayed, N. J.* "Soluble Epoxide Hydrolyase Dimerization is Required for Hydrolase Activity" *J. Biol. Chem.* **2013**, *288*, 7697-703.
27. Li, B. X.; Yamanaka, K.; **Xiao, X.*** "Structure-activity Relationship Studies of Naphthol AS-E and Its Derivatives as Anticancer Agents by Inhibiting CREB-mediated Gene Transcription" *Bioorg. Med. Chem.* **2012**, *20*, 6811-6820.
28. Jiang, M.; Li, B. X.; Xie, F.; Delaney, F.; **Xiao, X.*** "Design, Synthesis and Biological Evaluation of Conformationally Constrained Analogs of Naphthol AS-E as Inhibitors of CREB-mediated Gene Transcription" *J. Med. Chem.*, **2012**, *55*, 4020-4024.

29. **Xiao, X.;*** Li, B. X.; Mitton, B.; Ikeda, A.; Sakamoto, K. M. "Targeting CREB for Cancer Therapy: Friend or Foe" *Current Cancer Drug Targets,* **2010,** *10,* 384-391.
30. Li, B. X.; **Xiao, X.*** "Discovery of a Small Molecule Inhibitor of KIX-KID Interaction" *ChemBioChem* **2009**, *10*, 2721-2724.
31. Lim, H.; Reddy, M. M.; **Xiao, X.;** Wilson, J.; Wilson, R.; Connell, S.; Kodadek, T.* "Rapid Identification of Improved Protein Ligands Using Peptoid Microarrays" *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3866-3869.
32. Lee, J.; Yu, P.; **Xiao, X.;** Kodadek, T.* "A general system for evaluating the efficiency of chromophore-assisted light inactivation (CALI) of proteins reveals Ru(II) tris-bipyridyl as an unusually efficient warhead" *Mol. BioSyst.*, **2008**, *4,* 59-65.
33. **Xiao, X.**; Yu, P.; Lim, H.; Sikder, D.; Kodadek, T.* "Design and Synthesis of a Cell Permeable Synthetic Transcription Factor Mimic" *J. Comb. Chem.,* **2007,** *9,* 592-600**.**
34. **Xiao, X.**; Yu, P.; Lim, H.; Sikder, D.; Kodadek, T.* "A Cell-Permeable Synthetic Transcription Factor Mimic" *Angew. Chem. Int. Ed.*, **2007**, *46*, 2865-2868. (This is a **VIP paper** and highlighted in *Chemical & Engineering News*, **2007**, *85* (8), pp34 and *Nature*, **2007**, *446*, pp472 and *ChemBiochem* **2007**, *8*, 1095).
35. Alluri, P.; Liu, B.; Yu, P.; **Xiao, X.**; Kodadek, T.* "Isolation and Characterization of Coactivator-binding Peptoids from a Combinatorial Library" *Mol. BioSyst.* **2006**, *2*, 568-579.
36. **Xiao, X.** "More ways to combat bacterial infections" *Mol. BioSyst.*, **2006**, *2,* 91-92.
37. **Xiao, X.**; Morrell, A.; Fanwick, P.; Cushman, M.* "On the Mechanism of Conversion of 4-Carboxy-3,4-dihydro-3-phenyl-1(2*H*)-isoquinolones to Indeno[1,2-*c*]isoquinolines by Thionyl Chloride" *Tetrahedron*, **2006**, *62*, 9705-9712.
38. **Xiao, X.** "New insights into the molecular pathogenesis of Alzheimer's disease" *Mol. BioSyst.*, **2006**, *2,* 284-285.
39. **Xiao, X.**; Antony, S.; Pommier, Y.; Cushman, M.* "Total Synthesis and Biological Evaluation of 22-Hydroxyacuminatine" *J. Med. Chem.* **2006**, *49*, 1408-1412.
40. **Xiao, X.**; Cushman, M.* "Effect of E-ring Modifications in Camptothecin on Topoisomerase I Inhibition: A Quantum Mechanics Treatment" *J. Org. Chem.* **2005**, *70*, 9584-9587.
41. Li, S.; **Xiao, X.**; Yan, X.; Liu, X.; Xu, R.; Bai, D.* "A Convergent and Stereoselective Synthesis of a *seco*-Precursor of Macrolactin A" *Tetrahedron* **2005**, *61*, 11291-11298.
42. **Xiao, X.**; Li, S.; Yan, X.; Liu, X.; Xu, R.; Bai, D.* "Synthesis of a *seco*-Precursor and Analogues of Macrolactin A" *Chem. Lett.* **2005**, *34*, 906-907.
43. **Xiao, X.**; Cushman, M.* "A Facile Method to Transform trans-4-Carboxy-3,4-dihydro-3-phenyl-1(2*H*)-isoquinolones to Indeno[1,2-*c*]isoquinolines" *J. Org. Chem.* **2005**, *70*, 6496-6498.

44. **Xiao, X.**; Cushman, M.* "An ab initio Quantum Mechanics Calculation that Correlates with Ligand Orientation and DNA Cleavage Site Selectivity in Camptothecin-DNA-Topoisomerase I Ternary Cleavage Complexes" *J. Am. Chem. Soc.* **2005**, *127*, 9960-9961.
45. **Xiao, X.**; Miao, Z.; Antony, S.; Pommier, Y.; Cushman, M.* "Dihydroindenoisoquinolines Function as Prodrugs of Indenoisoquinolines" *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2795-2798.
46. **Xiao, X.**; Antony, S.; Pommier, Y.; Cushman, M.* "On the Binding of Indeno[1,2-*c*]isoquinolines in the DNA-Topoisomerase I Cleavage Complex" *J. Med. Chem.* **2005**, *48*, 3231-3238.
47. **Xiao, X.**; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M.* "Novel Autoxidative Cleavage Reaction of 9-Fluoredenes Discovered during the Synthesis of a Potential DNA-Threading Indenoisoquinoline" *J. Org. Chem.* **2004**, *69,* 7495-7501.
48. **Xiao, X.**; Fanwick, P. E.; Cushman, M.* "Synthesis, Crystal Structure and Conversion of the Polycyclic Trisanhydrotetramer of *o*-Aminobenzaldehyde to $Cu(TAAB)^{2+}$" *Syn. Comm.* **2004***, 34,* 3901-3907.
49. **Xiao, X.**; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M.* "Design, Synthesis, and Biological Evaluation of Cytotoxic 11-Aminoalkenylindenoisoquinoline and 11-Diaminoalkenylindenoisoquinoline Topoisomerase I Inhibitors" *Bioorg. Med. Chem.* **2004**, *12*, 5147-5160.
50. Nagarajan, M.; **Xiao, X.**; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M.* "Design, Synthesis, and Biological Evaluation of Indenoisoquinoline Topoisomerase I Inhibitors Featuring Polyamine Side Chains on the Lactam Nitrogen" *J. Med. Chem.* **2003**, *46,* 5712-5724.
51. Fox, B. F.; **Xiao, X.**; Antony, S.; Kohlhagen, G.; Pommier, Y.; Staker, B. L.; Stewart, L.; Cushman, M.* "Design, Synthesis, and Biological Evaluation of Cytotoxic 11-Alkenylindenoisoquinoline Topoisomerase I Inhibitors and Indenoisoquinoline-Camptothecin Hybrids" *J. Med. Chem.* **2003**, *46*, 3275-3282.
52. Xia, Y.; **Xiao, X.**; He, X.; Bai, D.* "The Unexpected Reductive Product of δ-Alkoxyenal by Sodium Borohydride in Methanol with Trace Magnesium Methoxide" *Chin. Chem. Lett.* **2002**, *13*, 809-810.
53. **Xiao, X**.; Bai, D.* "An Efficient and Selective Method for Hydrolysis of Acetonides" *Synlett* **2001**, 535-537.
54. Li, S.; Xu, R.; **Xiao, X**.; Bai, D.* "A Stereoselective Synthesis of the C3-C13 and C14-C24 Fragments of Macrolactin A" *Chin. J. Chem.* **2000**, *18*, 910-923.

Scientist Reviewer

Journal Reviewer:

Chemical Science, Cancer Research, Journal of the American Chemical Society, Journal of Medicinal Chemistry, Journal of Organic Chemistry, MedChemComm, ACS Chemical Biology, Chemistry-A European Journal, European Journal of Medicinal Chemistry, Chemical Research in Toxicology, Journal of Molecular Structure: THEOCHEM, Bioorganic & Medicinal Chemistry, Bioorganic & Medicinal Chemistry Letters, Protein & Peptide Letters, Journal of Oncology, Neuroendocrinology, PLOS One, Tumor Biology, Oncotarget, Journal of Biomolecular Screening, Current Medicinal Chemistry, Anti-Cancer Agents in Medicinal Chemistry

Grant Reviewer*:*

2008-2010: Alzheimer's Association grant applications
2009-2010: Maryland Industrial Partnerships program grant applications
2012: Department of Defense Breast Cancer Research Program study section
2014: Department of Defense Breast Cancer Research Program study section (invited, but declined due to COI)
2015: Department of Defense Breast Cancer Research Program study section
2015: NIH Synthetic and Biological Chemistry A (SBCA) study section
2016: French National Research Agency (consortium grant applications)
2016: Department of Defense Breast Cancer Research Program study section
2017: French National Research Agency (consortium grant applications)
2017a: Oregon Medical Research Foundation study section
2017: Oregon Tartar Trust Fellowship applications study section
2017: NIH Drug Discovery and Molecular Pharmacology (DMP) study section
2017b: Oregon Medical Research Foundation study section
2018-2022: Standing Member, NIH Drug Discovery and Molecular Pharmacology (DMP) study section
2019: Reviewer, University of Sharjah, United Arab Emirates

Editorial Boards

Journal of Cancer Science & Therapy	Editorial Board	2010-present
Journal of Cancer Research and Therapeutic Oncology		2013-present

Research Support

ACTIVE RESEARCH SUPPORT

R01 CA197513	$228,750 (ADC)	8/1/2017-7/31/2022

Role: PI
Title: Chemical Modulators of Nuclear Lamins
The goal of this application is to develop small molecule modulators of nuclear lamins to modulate DSB repair.

R01 CA197513-S1 $182,141 (DC) 3/1/2020-7/31/2022
Role: PI
Title: Chemical Modulators of Nuclear Lamins
The goal of this supplement is to support Dr. Francis Dhoro.

R01 GM122820 $221,000 (ADC) 4/1/2017-3/31/2021
National Institutes of Health
Title: Targeting Hsp60 to Inhibit CREB-mediated Gene Transcription
Role: PI
The goal of this application is to develop small molecule inhibitors of CREB by targeting Hsp60.

R21CA220061 $275,000 (DC) 8/01/2017—7/31/2020 (NCE)
National Institutes of Health
Role: PI
Title: *Targeting EWS-ATF1 for CCSST*

R21EB028425 $400,000 (DC) 4/1/2020-3/31/2023
National Institutes of Health (PI: Bingbing Li)
Role: co-I
Title: *Chemical Tools to Decode Nuclear Lamina-ome*

Murdock Charity Trust $120,000 (DC) 9/1/2018-8/31/2020
Title: A novel therapy for high-grade serous ovarian cancer
Role: PI

R01 CA186241 $240,000 (ADC) 4/1/2015-3/31/2020
National Institutes of Health
Title: Deubiquitination regulation of c-Myc (PI: Sears and Dai)
Role: co-I
The goal of this application is to understand the roles of deubiquitinase USP36 in regulating c-Myc.

Patent Applications

1. **Xiao, X.;** Li, B. X. "Naphthamides as Anticancer Agents" International Patent Number WO 2010048302 (notice of allowance from USPTO was issued on

9/27/2013).

2. **Xiao, X.;** Li, B. X.; Xie, F. "Pharmaceutical Compositions Comprising Naphthamides" PCT/US12/63361 (filed on 11/2/2012) (notice of allowance from USPTO was issued on 3/13/2015).
3. **Xiao, X.;** Chen, J.; Li, B. X. "Pyrroloquinazoline Compounds" PCT/US14/43265 (filed on 06/19/2014).
4. **Xiao, X;** Chao, Bo, Li, B. X. "Novel Acylated Pyrroloquinazolines" US Provisional application (filed on 5/9/2017).
5. **Xiao, X.**; Xie, F.; Li, B. X. "SYNERGISTIC INHIBITORS OF CREB-MEDIATED GENE TRANSCRIPTION" Provisional application (filed on 10/24/2019).

Issued Patents

1. **Xiao, X.;** Li, B. X. "Naphthamides as Anticancer Agents" (US patent 8,653,086 issued on 2/18/14) (licensed to Transmed Oncology, Inc.).
2. **Xiao, X.;** Li, B. X.; Xie, F. "Pharmaceutical Compositions Comprising Naphthamides" (US patent 9,073,820 issued on 7/7/15).
3. **Xiao, X.;** Chen, J.; Li, B. X. "Pyrroloquinazoline Compounds" (US patent 9,133,203 issued on 9/15/15).