## BIOGRAPHICAL SKETCH

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NAME: Wei Li

eRA COMMONS USER NAME (credential, e.g., agency login): Weili2

POSITION TITLE: Distinguished Professor and Director of UTCoP Drug Discovery Center
Founder and CSO, SEAK Therapeutics, LLC

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| University of Science and Technology of China | B.S. | 07/1992 | Chemistry |
| Columbia University in the City of New York | Ph.D. | 07/1999 | Chemistry |

**A. Personal Statement:**

A chemist by training, I have developed significant expertise in chemical biology and small molecule anti-cancer drug discovery over the past 20 years. My lab is equipped with software for computer aided drug design, equipment for medicinal chemistry studies, complete cell culture labs, and equipment for biological investigations of drug actions. I have developed several approved animal protocols for pharmacokinetics (PK), *in vivo* efficacy and toxicity studies.

We discovered a new generation of tubulin inhibitors targeting the colchicine-binding site, represented by the current investigational new drug **Sabizabulin** (earlier names as VERU-111 or ABI-231, originally designed and synthesizedin my lab). The VERU-111 scaffold has been comprehensively patented (WO2011/109059 and WO2012/027481) and licensed to Veru Inc. for commercial development. VERU-111 has recently succeeded in two Phase 2 clinical trials (NCT03752099 and NCT04388826). These clinical trials showed that Sabizabulin is well-tolerated and has promising clinical efficacy and good safety profiles. A Phase 3 clinical trial with Sabizabulin (NCT04844749, VERACITY) in men with advanced metastatic castration resistant prostate cancer is currently ongoing. Interestingly, an ongoing Phase 3 trial of VERU-111 in severely ill COVID-19 patients (NCT04842747) showing promising efficacy in reducing hospitalized COVID-19 patient death by 55% compared with placebos, and Veru submitted an Emergency Use Authorization (EUA) of sabizabulin to the FDA for hospitalized COVID-19 patients on 6/7/2022.

I am also the Founder and CSO of my startup company, SEAK Therapeutics LLC, to develop potential new targeted small molecule drugs for pediatric cancers and neurodegenerative diseases. As a medicinal chemist, my dream goal is to collaborate with biologists and partner with industry to help to bring a new targeted drug to the market to benefit patients.

*Customize for specific grant application need here*

**Currently ongoing projects:**

R01CA148706 (NCI) Li (contact PI), Miller (MPI) 1/2011-6/2026
Targeting the colchicine site in tubulin for cancer therapy

R01CA240447 (NCI) Li (contact PI), Zhou (MPI) 7/2020-6/2025
Dual inhibition of MDM2 and XIAP as a therapeutic strategy in cancer

RF1AG072703 (NIA) Liao (contact PI); Li, Bhaskar (MPIs) 6/2022-5/2027
Validation of a novel tau clearance mechanism

R61/R33NS124923 (NINDS) Jiang (contact PI), Li (MPI) 12/2021-11/2024
Targeting TRPC3 Channels for Epileptic Seizures

BC190092 (DoD) Li (PI), Seagroves (Partner PI) 3/2020-2/2023
W81XWH2010011: PI's project (Li)
W81XWH2010019: Partner PI's project (Seagroves)
Discovery of orally bioavailable tubulin inhibitors to overcome taxane resistance in metastatic breast cancer

1R24EY029950 (NEI) Role: Co-I (PI: Monica Jablonski) 3/2020-2/2025
Novel extended release glaucoma therapy for once daily dosing.

R43CA257324 (NCI) Wu (contact PI), Li (MPI) 9/2020-8/2022
Feasibility study of developing SEAK-114 for the treatment of pediatric cancers

**B. Positions, Scientific Appointments, and Honors**

**Positions and Scientific Appointments**

2020-present UTHSC Distinguished Professor
2018-present Founder and CSO, SEAK Therapeutics LLC
2017-present Director, UTHSC College of Pharmacy Drug Discovery Center, UTHSC, Memphis, TN
2016-present Vice President and Executive Committee Member, MALTO Medicinal Chemistry.
2015-present Member of American Society for Pharmacology and Experimental Therapeutics (ASPET)
2015-2017 Secretary and Executive Committee Member, American Chemical Society Memphis Section
2014-2020 Professor and Faculty Director of Shared Instrument Facility, UTHSC, Memphis, TN
2009-2014 Associate Professor with tenure, UTHSC, Memphis, TN
2004-present Member of American Association for Cancer Research (AACR)
2004-2009 Tenure track Assistant Professor, UTHSC, Memphis, TN
2001-2004 Non-tenure track Assistant Professor, UTHSC, Memphis, TN
1999-2001 Instructor, University of Tennessee Health Science Center, Memphis, TN
1998-present Member of American Chemical Society (ACS)
1994-1999 Graduate Research Assistant, Department of Chemistry, Columbia University, New York, NY
1992-1994 Research Assistant, Dalian Inst. of Chem. Phys., the Chinese Academy of Sciences, China.
1987-1992 Undergraduate Research, University of Science and Technology of China, China

**Honors**

2022 2022 Health Care Heroes Award in Innovation, the Memphis Business Journal
2015 Outstanding Alumni Lecturer, Dalian Inst. of Chem. Phys., the Chinese Academy of Sciences
2012, 2014 Research Award, University of Tennessee Research Foundation
2010, 2014 University of Tennessee Research Foundation Innovation Awards
1986 First Prize in National Young Chemist Competition for Chemistry Olympia, China

**Journal and Grant Reviewer**

Journal reviewer: Journal of American Chemical Society; Bioorganic Medicinal Chemistry Letters; Bioorganic Medicinal Chemistry; The Open Magnetic Resonance Journal; Molecular Diversity; European Journal of Medicinal Chemistry; Journal of Medicinal Chemistry; International Journal of Nanomedicine; PLoS One; Anti-cancer Agents in Medicinal Chemistry; Royal Society of Chemistry Journals; Medicinal Research Reviews; Molecule Cancer Therapeutics; Cancer Research; Oncotarget; Scientific Reports; Pharmacological Reviews, Molecular Cancer Research; Chemical Sciences; PNAS; Nature.

Grant reviewer: NIH (2011/07: ZRG1 BCMB-U 30; 2012/03: ZRG1 BCMB-R 30; 2012/07: BCMB I; 2012/11: NCI SBIR/STTR; 2014/03: NCI SBIR/STTR; 2014/07: NCI SBIR/STTR; 2015/03: NCI SBIR/STTR; 2015/06:NCI SBIR/STTR; 2015/12: NCI SBIR/STTR; 2016/01: NCI ZRG1 OTC-Y (02) M; 2016/03: NCI SBIR/STTR; 2016/09: NCI ZRG-OTC K(04); 2016/11: NCI SBIR/STTR; 2016/12: NCI SBIR/STTR; 2017/03: NCI SBIR/STTR; 2017/10: ZRG1 BCMB-D; 2017/10: ZRG1 BCMB-N; 2018/03, NCI SBIR/STTR; 2018/07, ZRG1 IDM-C(50)R; 2018/11, NCI SBIR/STTR; 2019/10-12, NIH, ZRG1-MOSS-R70, NIH Director's DP2 Award-2020; 2020/03, NCI, OTC-T SBIR/STTR; 2020/10-12, NIH Director's DP2 Award-2021; 2021/10, EBIT; 2021/10-12, NIH Director's DP2 Award-2022; 2022/06, NCI CDDT SBIR/STTR).

American Chemical Society; Human Frontier Science Program; National Science Foundation; Florida Department of Health; Estonian Science Foundation; US Army. Oklahoma Center for the Advancement of Science & Technology (OCAST); Czech Science Foundation; Health Research Council of New Zealand; The Cancer Society of New Zealand; Prostate Cancer UK; French National Cancer Institute (INCa).

**Editorial Appointment:**

Guest editor, *Pharmaceutical Research*, Theme Issue on drugs targeting tubulin inhibitors, Vol 29, 2012.
Guest editor, *Molecules*, Theme issue on Tubulin Inhibitors, 2017. Special Issue on Tubulin Inhibitors, 2020; Special Issue to honor Dr. Duane Miller, 2020.
Guest editor, *Acta Pharmaceutica Sinica B*, Theme Issue on drug targeting and resistance, 2018.
Editorial Board and Section Editor (Anti-Cancer Agent section): *Current Medicinal Chemistry*, 2014-present.
Editorial Board member, *Acta Pharmaceutica Sinica B*, 2016-present; *Molecules*, 2018-present; *Genes & Diseases*, 2018-present; *Cancer Letters*, 2020-present.

**Issued and Licensed Patents (listed for the 13 US patents only):**

- Thiazolidinone amides, thiazolidine carboxylic acid amides, and serine amides, including polyamine conjugates thereof, as selective anti-cancer agents, US 7,662,842 B2, issued on 2/16/2010.
- Compounds for treatment of cancer, US 8,592,465, issued on 11/26/2013; US 8,822,513, issued on 9/2/2014; US 9,029,408, issued on 5/12/2015; US 9,334,242, issued on 5/10/2016; US 9,447,049, issued on 9/20/2016; US 9,981,915, issued on 5/29/2018; US 10,022,356, issued on 7/17/2018; US 10,155,728, issued on 12/18/2018; US 10,301,285, issued on 5/28/2019; US 10,525,037, issued on 1/7/2020; US 15/872,199, allowed on 7/31/2020 (all licensed to Veru Inc.)

**C. Contribution to Science (187 peer reviewed papers, 13 issued US patents and 5 book chapters)**

1. **Determine effects of confined environments on photochemical reactions.** When I was a graduate student at the chemistry department of Columbia University working under the direction of Professor Nick Turro, I contributed to elucidate the effects of confined environments on photochemical reactions.

   a. **Wei Li**, Xuegong Lei, George Lem, Ann McDermott, Nicholas J. Turro, Nils Bottke and Waldemar Adam, "Oxygen and structural effect on silicalite $^{29}$Si spin-lattice relaxation studied by high resolution $^{29}$Si solid state NMR", **Chem. Mater.**, 12, 731-737 (**2000**).

   b. Nicholas J. Turro, Xue-Gong Lei, **Wei Li**, Zhiqiang Liu, and M. Francesca Ottaviani, "Adsorption of Cyclic Ketones on the External and Internal Surfaces of a Faujasite Zeolite (CaX). A Solid-State $^{2}$H NMR, $^{13}$C NMR, FT-IR, and EPR Investigation", **J. Am. Chem. Soc.**, 122, 12571-12581 (**2000**).

   c. Takashi Hirano, **Wei Li**, Lloyd Abrams, Paul J. Krusic, M. Francesca Ottaviani and N. J. Turro, "Reversible Oxygenation of a Diphenylmethyl Radical Rendered Supramolecularly Persistent" **J. Am. Chem. Soc**.,121, 7170-7171 (**1999**).

   d. Nicholas J. Turro, Ann McDermott, Xuegong Lei, **Wei Li**, Lloyd Abrams, M. Francesca Ottaviani, Hege Stogard Beard, Kendall N. Houk, Brett R. Beno and Patrick S. Lee, "Photochemistry of ketones adsorbed on size/shape selective zeolites. A superamolecular approach to persistent carbon centered radicals", **Chem. Commun**., 697-698 (**1998**).

2. **Discovery and development of a new generation of tubulin inhibitors for cancer therapy.** Starting from my independent academic career in 2004, I have worked towards the goal of developing a useful therapeutic agent. One major area that I have been working on is to develop a new generation of orally bioavailable tubulin inhibitors. In the past 10+ years, we have discovered novel series of orally bioavailable tubulin inhibitors targeting the colchicine binding site and their targeted delivery to tumor cells. We have recently obtained high-resolution crystal structures of tubulin protein with more than 15 of our potent compounds and the deposition of the PDBs are ongoing (PDB: 5H7O, 6BR1, 6BRF, 6BRY, 6BS2, 6C47, 6C4B, 6C7U, and 6D88). I have been serving as the primary investigator in these studies.

   a. Kinsie Arnst, Yuxi Wang, Dong-Jin Hwang, Yi Xue, Terry Costello, David Hamilton, Qiang Chen, Jinliang Yang, Frank Park, James T. Dalton, Duane D. Miller, and **Wei Li**, “A potent, metabolically stable tubulin inhibitor targets the colchicine binding site and overcomes paclitaxel drug resistance”, **Cancer Res**, 78(1):265-277, **(2018)**. PMID: 29180476, PMCID: Journal-in-progress.

   b. Qinghui Wang, Kinsie E. Arnst, Yuxi Wang, Gyanendra Kumar, Dejian Ma, Hao Chen, Jinliang Yang, Stephen W. White, Duane D. Miller, **Wei Li**, “Structural modification of the 3,4,5-trimethoxyphenyl moiety in the tubulin inhibitor VERU-111 leads to improved antiproliferative activities”, **J. Med. Chem.**, 61(17):7877-7891, (**2018**). PMID: 30122035, PMCID: PMC6637749.

   c. Hao Chen, Shanshan Deng, Yuxi Wang, Najah Albadari, Gyanendra Kumar, Dejian Ma, Weimin Li, Stephen W. White, Duane D. Miller, and **Wei Li**, “Structure Activity Relationships Study of Novel 6

Aryl-2-Benzoyl-Pyridines as Tubulin Polymerization Inhibitors with Potent Antiproliferative Properties", **J Med Chem,** 63(2):827-846**, (2020),** PMID: 31860298, PMCID: Journal-in-progress.

d. S Deng, RI Krutilina, KL Hartman, H Chen, DN Parke, R Wang, F Mahmud, D Ma, PB Lukka, B Meibohm, TN Seagroves, DD Miller, and W Li, "Colchicine-Binding Site Agent CH-2-77 as a Potent Tubulin Inhibitor Suppressing Triple-Negative Breast Cancer", **Mol Cancer Ther**, **2022**, in press, doi: 10.1158/1535-7163.MCT-21-0899

3. **Discovery of non-calcemic vitamin D analogs for autoimmune diseases**. Another area I have been working on is to develop tissue selective, non-hypercalcemic vitamin D analogs as potential anti-inflammatory or cancer prevention agents. My initial contributions were the elucidation of structures for a large number of novel vitamin D metabolites by P450scc enzymes. Subsequently, we designed strategies to stereo-specifically synthesize biologically active metabolites identified. We have also been working to synthesize new analogs to further improve their drug-like properties without causing hypercalcemia at doses well above potential therapeutic doses.

a. Zongtao Lin, Srinivasa Reddy Marepally, Dejian Ma, Linda K. Myers, Arnie E. Postlethwaite, Robert C. Tuckey, Tae-Kang Kim, Junming Yue, Andrzej T. Slominski, Duane D. Miller, **Wei Li**, "Chemical synthesis and biological activities of 20S,24S/R-dihydroxyvitamin D3 epimers and their 1α-hydroxyl derivatives", **J. Med. Chem.**, 58(19):7881-7887, (**2015)**. PMID: 26367019 PMCID: PMC4613797

b. Zongtao Lin, Srinivasa R. Marepally, Dejian Ma, Tae-Kang Kim, Allen SW. Oak, Linda K. Myers, Robert C. Tuckey, Andrzej T. Slominski, Duane D. Miller, **Wei Li**, "Synthesis and Biological Evaluation of the Active Vitamin D3 Metabo-lite 20S,23S-Dihydroxyvitamin D3 and Its 23R Epimer", **J. Med. Chem.**, 59 (10): 5102–5108, (**2016)**. PMID: 27070779, PMCID: PMC5330258.

c. Zongtao Lin, Hao Chen, Anna Y. Belorusova, John C. Bollinger, Edith K.Y. Tang, Zorica Janjetovic, Tae-Kang Kim, Zhongzhi Wu, Duane D. Miller, Andrzej T. Slominski, Arnold E. Postlethwaite, Robert C. Tuckey, Natacha Rochel, and **Wei Li**, "1α,20S-Dihydroxyvitamin D3 Interacts with Vitamin D Receptor: Crystal Structure and Route of Chemical Synthesis", **Sci. Rep.**, 7:10193, (**2017).** PMID: 28860545 PMCID: PMC5579064.

d. Lin Z, Marepally SR, Goh ESY, Cheng CYS, Janjetovic Z, Kim TK, Miller DD, Postlethwaite AE, Slominski AT, Tuckey RC, Peluso-Iltis C, Rochel N, **Li W**, "Investigation of 20S-hydroxyvitamin D3 analogs and their 1α-OH derivatives as potent vitamin D receptor agonists with anti-inflammatory activities", **Sci. Rep**., 8:1478, (**2018**). PMID: 29367669 PMCID: PMC5784132.

4. **Discovery of small molecule selective survivin inhibitors**. My lab recently discovered a unique scaffold for selective survivin inhibition. Survivin is an anti-apoptotic protein that is highly expressed in most tumor cells and during embryonic and fetal development, but has very low expression in adult differentiated cells. We are currently perform structure based drug design on this project.

a. Jin Wang and **Wei Li**, "Discovery of Novel SMAC Mimetics as Selective IAP Inhibitors", **J Pharm Exp Ther**, 349(2):319-29, (**2014**). PMID: 24623800, PMCID: PMC3989805.

b. Wu Z, Gu L, Zhang S, Liu T, Lukka PB, Meibohm B, Bollinger JC, Zhou M, **Li W.** "Discovery of N-(3,4-Dimethylphenyl)-4-(4-isobutyrylphenyl)-2,3,3a,4,5,9b-hexahydrofuro[3,2-c]quinoline-8-sulfonamide as a Potent Dual MDM2/XIAP Inhibitor". **J Med Chem**., 64:1930-1950, (**2021**). PMID: 33556244.

c. Qinghui Wang, Kinsie E. Arnst, Yi Xue, Zi-Ning Lei, Dejian Ma, Zhe-Sheng Chen, Duane D. Miller, **Wei Li**, "Synthesis and biological evaluation of indole-based UC-112 analogs as potent and selective survivin inhibitors", **Eur. J. Med. Chem.**, 149:211-224, (**2018**). PMID: 29501942 PMCID: PMC5849576.

d. Najah Albadaria, Shanshan Deng, Hao Chen, Guannan Zhao, Junming Yue, Sicheng Zhang, Duane D. Miller, Zhongzhi Wu, **Wei Li**, "Synthesis and biological evaluation of selective survivin inhibitors derived from the MX-106 hydroxyquinoline scaffold", **Eur. J. Med. Chem.**, 224:113719, (**2021**). PMID: 34371464, PMCID: PMC8511083.

5. **Collaboration with researchers in other biomedical fields using expertise in chemistry**. I have also contributed to other projects using my expertise in analytical chemistry and medicinal chemistry. These efforts have resulted in joint papers in various biomedical research fields outside my own research focus.

a. Ajeeth K. Pingili, Mehmet Kara, Nayaab Khan, Anne M. Estes, Zongtao Lin, **Wei Li**, Frank J. Gonzalez and Kafait U. Malik. “6β-Hydroxytestosterone, a Cytochrome P450 1B1 Metabolite of Testosterone Contributes to Angiotensin II-Induced Hypertension and its Pathogenesis in Male Mice”, **Hypertension**, 67:916-26, (**2016**). PMID: 26928804, PMCID: PMC4833582.

b. Wang B, Liu Y, Huang L, Chen J, Li JJ, Wang R, Kim E, Chen Y, Justicia C, Sakata K, Chen H, Planas A, Ostrom RS, **Li W,** Yang G, McDonald MP, Chen R, Heck DH, Liao FF. A CNS-permeable Hsp90 inhibitor rescues synaptic dysfunction and memory loss in APP-overexpressing Alzheimer's mouse model via an HSF1-mediated mechanism. **Mol Psychiatry**, 22:990-1001, **(2017)**. PMID: 27457810, PMCID: PMC5323357

c. Zhousheng Xiao, Jerome Baudry, Li Cao, Jinsong Huang, Hao Chen, Charles R. Yates, **Wei Li**, Christopher M. Waters, Jeremy C. Smith, L. Darryl Quarles, “Polycystin-1 interacts with TAZ to stimulate osteoblastogenesis and inhibit adipogenesis”, **J Clin Investig**, 128(1): 157-174, (**2018**). PMID: 29202470, PMCID: PMC5749530.

d. Bhattarai RS, Kumar V, Romanova S, Bariwal J, Chen H, Deng S, Bhatt VR, Bronich T, **Li W**, Mahato RI. "Nanoformulation design and therapeutic potential of a novel tubulin inhibitor in pancreatic cancer". **J Control Release**. **2021**, 329:585-597. PubMed PMID: 33010334. PMCID: PMC7904572.

**Complete List of Published Work in MyBibliography:**
http://www.ncbi.nlm.nih.gov/sites/myncbi/wei.li.11/bibliography/45414079/public/?sort=date&direction=descending