CHENG HU

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SUMMARY

Innovative and productive drug discovery project lead with extensive experience in molecular design and drug development, ML model development and implementation, and drug discovery portfolio management.

Demonstrated abilities to:

- Lead cross-functional team to build drug discovery project portfolio, formulate project goals and implement execution plans;
- Manage and maintain productive relationships with internal stakeholders (biology, data science, engineering, ADMET-PK) and external CROs.
- Manage and coach medicinal chemistry/project team members;
- Lead the development and implementation of machine learning models to enable faster delivery of hit2lead and lead optimization project goals;
- Lead the evaluation, selection and implementation of computational tools to expedite compound design/make/test/analysis (DMTA) cycle;

PROFESSIONAL EXPERIENCE AND ACHIEVEMENTS

INDEPENDENT CONSULTANT **02/2024 to Now**

- Advise companies on developing ML models for ADMET prediction, structure-based pKi predictions, and generativeAI de novo small molecules discovery.
- Advise startup biotech companies on implementation of AI workflows to identify novel chemotypes, expedite hit2lead and LO, and de-risk preclinical & clinical development.

ATOMWISE INC. SAN FRANCISCO, CA

Associate Director, Medicinal Chemistry, AI Drug Discovery **04/2021 to 01/2024**

Molecular Design and Drug Development (M3D)

- Delivered best-in-class systemic and first-in-class gut-restricted RIPK2 advanced candidates for IBD
- Launched the design and synthesis of two hit to lead projects (undisclosed oncology/immunology targets)
- Led multiple AI enabled HitID, HitExpansion, Hit2Lead and LeadOptimization drug discovery projects;
- Contributed to the identification and prioritization of projects to build a portfolio of drug discovery projects.

AI Drug Discovery Tool Development:

- Represented medicinal chemistry/DMPK on the weekly AIDD model and workflow development meetings
- Advised development and implementation of ADMETwise for internal and collaborative drug discovery projects
- Led the integration of ADMETwise and Structure-based pKi prediction into the automatic molecule design/synthesis/test/analysis workflow
- Built the practical use cases of AI application in drug discovery process for BD purposes

DENALI THERAPEUTICS, SOUTH SAN FRANCISCO, CA

Senior Scientist, Project Team Lead **10/2016 to 03/2021**

- Led 3 medicinal chemistry campaigns (NLRP3, DLK/LZK and RIPK1) in the neuroinflammation field to achieve advanced candidate or development candidate milestones;
- Led the synthesis team of multiple internal chemists and an external chemistry team (6-14 FTEs) at CRO for the timely delivery of relevant targets;
- Led the structure-based drug design discussions on the target design meetings;
- Maintained a productive relationship with biochemistry, structure biology, computational chemistry and cell biology team for the compounds test, assay development/modification, pharmacophore modeling and biophysics characterizations.

NURIX INC, SAN FRANCISCO, CA

Scientist, Project Team Lead **08/2015-10/2016**

- Led a hit to lead medicinal chemistry campaign in the protein-protein interaction target field, achieved over 2000 folds of potency improvement by applying structure-based drug design approaches;
- Led the synthesis team of 3 internal chemists and an external chemistry team (4-6 chemists) at 2 different CROs for the timely delivery of relevant targets;
- Led the structure-based drug design utilizing LiveDesign, FEP calculation and MD simulation;
- Designed sp3-rich DEL templates for the development of in-house DEL libraries;
- Contributed to pivoting the medicinal chemistry to targeted protein degradation realm;

NOVARTIS INSTITUTE OF BIOMEDICAL RESEARCH, Emeryville, CA **01/2008-08/2015**

Scientist I

- Proposed and developed 2 novel inhibitor series featuring sp3 rich, low clogP and sub nanomolar activity
- Proposed and identified a “methyl pocket” to improve kinase specificities;
- Established a novel synthesis route (shorten from 10 steps to 6 steps) to target compounds;
- Identified “sweetspot” region of cLogP, PKa, PSA to design compounds addressing efflux, HERG issues;
- Developed synthesis route to a novel building block with reduced efflux and enhanced metabolic stabilities;
- Developed a protecting method to enhance chirality and separation of key intermediate.

CHEMOCENTRYX INC, Mountain View, CA **04/2005-12/2007**

Senior Associate Scientist

- Developed enantioselective synthesis of C5a active enantiomer which lead to discovery of Avacopan;
- Designed and synthesized inhibitors on CCR2, CCR9, CXCR7, C5a chemokine receptor antagonists;
- Developed mid-scale (10-50 g) process of key compound synthesis to support preclinical studies;
- Documented and patented the proprietary structures of the new active compounds discovered.

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DISCOVERY PARTNERS INTERNATIONAL, South San Francisco, CA **01/2002-03/2005**

Research Associate II

- Developed high-throughput synthesis chemistry for the production of 12 drug discovery libraries which were shipped to customers to generate revenue of US$ 8 million, with average gross margin of 70%;
- Developed 96-well plate based synthesis and purification technologies for production of combinatorial libraries;

- Proposed and conducted initial feasibility studies of project ideas;

SHANGHAI VOLKSWAGEN, Shanghai, China **1998-2001**

Project Manager, 1998 - 2001

- Led a team of 5 engineers to prepare the process of a new painting workshop for the production of Volkswagen Polo model in China, including: process layout, testing and screening of materials from 12 vendors, process parameter determination and documentation.

EDUCATION

M. Eng. Fine Chemical Engineering, East China University of Science and Technologies **1998**
B.Sci. Chemistry**,** Nankai University **1995**

Activities

DEIB Committee, founding member and Head of DEIB training, Atomwise, Inc. **2022-2023**
Laboratory Safety Committee, ChemistryLab Safety Officer**,** Novartis (Emeryville) **2010-1014**

MEMBERSHIPS

American Chemical Society (Member Since 2003)
Sigma Xi (Full Member Since 2009)

LANGUAGE SKILLS

English, Chinese, Spanish (work proficient), German (work proficient)

REFERENCES

Available upon request

PUBLICATIONS

1. Bagdasarian, Alex L.; Craig, Robert A., II; De Vicente Fidalgo, Javier; Estrada, Anthony A.; Fox, Brian M.; **Hu, Cheng**; Huffman, Benjamin J.; Lexa, Katrina W.; Nilewski, Lizanne G.; Osipov, Maksim. NLRP3 antagonists for disease treatment WO 2023158708

2. Craig, Robert A; Fox, Brian M.; **Hu, Cheng**; de Vicente, Javier et al. Discovery of Potent and Selective DLK/LZK Inhibitors with Neuroprotective Properties in In Vitro and In Vivo Models of AML. Journal of medicinal chemistry (2022), 65(24), 16290-16312

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4. Bagdasarian, Alex L.; Bucher, Cyril; Craig, Robert A., II; De Vicente Fidalgo, Javier; Estrada, Anthony A.; Fox, Brian M.; **Hu, Cheng**; Huffman, Benjamin J.; Lexa, Katrina W.; Nilewski, Lizanne G.; Osipov, Maksim;

Thottumkara, Arun. Preparation of pyridazinone compounds as NLRP3 modulators, compositions and methods WO 2022006433

5. Ramurthy, Savithri; Taft, Benjamin R.; Aversa, Robert J.; Barsanti, Paul A.; Burger, Matthew T.; Lou, Yan; **Hu, Cheng;** et al. Design and discovery of N-(3-)2-(2-Hydroxyethoxy)-6-morpholineopyridine-4-yl)-4-methylphenhyl)-2-(trifluoromethyl)isonicotinamide, a Selective, Efficacious and Well-Tolerated RAF Inhibitor Targeting RAS Mutant Cancers: The Path to Clinic. Journal of medicinal chemistry (2020), 63(5), 2013-2027

6. Skepper Colin K; Moreau Robert J; Appleton Brent A; Benton Bret M; Drumm Joseph E 3rd; Feng Brian Y; Geng Mei; **Hu Cheng**; Li Cindy; Lingel Andreas. Discovery and Optimization of Phosphopantetheine Adenylyltransferase Inhibitors with Gram-Negative Antibacterial Activity. Journal of medicinal chemistry (2018), 61(8), 3325-3349

7. Bonanomi, Giorgio; Estrada, Anthony A.; Feng, Jianwen A.; Fox, Brian; Francini, Cinzia Maria; **Hu, Cheng**; Leslie, Colin Philip; Osipov, Maksim; Sudhakar, Anantha; Sweeney, Zachary K.. Preparation of hexahydropyrazolodiazepines as RIPK1 inhibitors WO 2018213634

8. De Vicente Fidalgo, Javier; Estrada, Anthony A.; Feng, Jianwen A.; Fox, Brian; Francini, Cinzia Maria; Hale, Christopher R. H.; **Hu, Cheng**; Leslie, Colin Philip; Osipov, Maksim; Serra, Elena. Preparation of substituted pyrazolopyrazolones for treating necrotic cell disease or an inflammatory disease WO 2018213632

9. Estrada, Anthony A.; Feng, Jianwen A.; Fox, Brian; **Hu, Cheng**; Osipov, Maksim; Sweeney, Zachary K.; De Vicente Fidalgo, Javier. Preparation of substituted pyrazolopyrazolones for treating necrotic cell disease or an inflammatory disease WO 201602083

10. Fidalgo, Javier de Vicente; **Hu, Cheng**; Li, Xiaolin; Lu, Peichao; Mergo, Wosenu; Mutnick, Daniel; Reck, Folkert; Rivkin, Alexey; Skepper, Colin Kevin; Wang, Xiaojing Michael; Preparation of quinolone derivatives as antibacterials that inhibit bacterial DNA gyrase WO 2016020836

11. Barsanti, Paul A.; Pan, Yue; Lu, Yipin; Jain, Rama; Cox, Matthew; Aversa, Robert J.; Dillon, Michael P.; Elling, Robert; **Hu, Cheng**; Jin, Xianming; et al; Structure-Based Drug Design of Novel, Potent, and Selective Azabenzimidazoles (ABI) as ATR Inhibitors ACS Med.Chem.Lett. Published online

12. Aversa, Robert; Barsanti, Paul A.; Burger, Matthew; Dillon, Michael Patrick; Dipesa, Alan; **Hu, Cheng**; Lou, Yan; Nishiguchi, Gisele; Pan, Yue; Polyakov, Valery; Bi-aryl amide compounds as kinase inhibitors and their preparation PCT Int. Appl. (2014), WO 2014151616

13. Antonios-McCrea, William R.; Barsanti, Paul A.; **Hu, Cheng**; Jin, Xianming; Lin, Xiaodong; Martin, Eric J.; Pan, Yue; Pfister, Keith B.; Renhowe, Paul A.; Sendzik, Martin; Preparation of pyridine biaryl amine compounds as CDK9 inhibitors PCT Int. Appl. (2012), WO 2012101066

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15. Abrams, Tinya; Barsanti, Paul A.; Ding, Yu; Duhl, David; Han, Wooseok; **Hu, Cheng**; Pan, Yue. Triazole compounds as KSP inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer. PCT Int. Appli. (2011), WO 2011128381.

16. Charvat, Trevor T.; **Hu, Cheng**; Melikian, Anita; Novack, Aaron; Pennell, Andrew M.K.; Powers, Jay; Punna, Sreenivas; Sullivan, Edward J.; Thomas, William D.; Ungashe, Solomon. Preparation of N-(2-(hetaryl)aryl) arylsulfonamides and N-(2-(hetaryl)hetaryl) arylsulfonamides as CCR9 receptor antagonists. PCT Int. Appl. (2009), WO 2009038847

17. Charvat, Trevor T.; **Hu, Cheng**; Melikian, Anita; Novack, Aaron; Pennell, Andrew M. K.; Sullivan, Edward J.; Tan, Xuefei; Thomas, William D.; Ungashe, Solomon; Zeng, Yibin. N-(Triazolylphenyl)-benzenesulfonamides as chemokine receptor antagonists, their preparation, pharmaceutical compositions, and use in therapy. PCT Int. Appl (2008), WO 2008010934

18. Melikian, Anita; Wright, John Jessen; Krasinski, Antoni; **Hu, Cheng**; Novack, Aaron. Prepararation of substituted 4-quinolones and naphthyridin-4-ones as chemokine receptor CCXCKR2 antagonists**.** PCT Int. Appl (2007), WO 2007059108.

19. **Cheng Hu**, Weihong Zhu, Wenqiang Lin, He Tian. 1999. Synthesis and luminescence of novel emitting copolymers, *Synthetic Metals* 102: 1129-1130.

20 **Hu, Cheng**; Zhu, Weihong; Tian, He. 1999. Synthesis of novel copolymeric dyad electroluminescent materials. *Acta Polymerica Sinica*. 2: 232-235.

21. Weihong Zhu, **Cheng Hu**, Kongchang Chen, He Tian. 1998. Luminescent properties of copolymeric dyad compounds containing 1,8-naphthalimide and 1,3,4-oxadiazole, *Synthetic Metals* 96: 151-154.