XIN XU, PH.D.

Redwood City, CA **dxuxin@hotmail.com** **785.8610.785**

CORE STRENGTHS

- **Expertise in Drug Discovery:** 2+ years of R&D experience in Bristol Myers Squibb in the division of Small Molecule Drug Discovery; Ph.D. in Biochemistry and Molecular Biophysics.
- **Hands-on Lab Expertise:** Single Crystal X-ray Diffraction Experiments; Assay Design & Target Validation; High-throughput Screening; Surface Plasmon Resonance (SPR); Protein Expression/ Refolding/ Purification.
- **Educational and Leadership Capacities:** Selected for Graduate Student Leadership Development Program; Graduate Teaching Assistant in Master & Ph.D.; the President of Student News Agency at College.
- **Advanced Analytical and Digital Proficiencies**: GraphPad; Instant JChem; ATLAS; PyMOL; PHENIX.
- **Distinguished Scholarly and Research Contributions:** Excellence in Biochemistry and Molecular Biophysics GRA Award; 2 publications recognized as Top Reads and gracing the cover of their respective issues.

PROFESSIONAL EXPERIENCE

(For research details, please refer to the last 2 pages.)

Scientist in Leads Discovery and Optimization Redwood City, CA Jan 2022-present

Bristol Myers Squibb, Division of Small Molecule Drug Discovery.

- Support the entire continuum of drug discovery from lead identification to clinical candidate delivery.
- Leverage state of the art technologies to deliver innovative and comprehensive preclinical *in vitro* datasets to support our drug discovery pipeline areas such as cell therapy, oncology, immunology, and cardiovascular diseases.
- Design, validate, execute, and interpretate biochemical and biophysical assays for lead discovery, molecular profiling and lead optimization, in support of our portfolio focused on targets in the tumor microenvironment.
- Collaborate across project teams to help shape the *in vitro* screening strategy, identify appropriate assay platforms, and develop high throughput assays using cutting-edge technologies and automation platforms.
- Among the 3 projects I have been worked on, all were forwarded from Pre GTS to GTS.

Graduate Research Assistant Manhattan, KS Aug 2019-Dec 2021

Kansas State University, Department of Biochemistry and Molecular Biophysics.

- Research on human complement molecules recognition and interactions.
- Expression, refolding, and purification of recombinant proteins and enzymes.
- X-ray Crystallization of proteins and protein-small molecule complexes.

Medical Laboratory Technician Hebei, China Nov 2012-Jul 2013

Second Hospital of Hebei Medical University, Clinic Laboratory.

- Immunohistochemical analysis for AIDS and Syphilis identification
- Identification of immature leukocytes from bone marrow by microscope for suspicious leukemia patients.
- Microbial culture by blood culture bottles to help physicians diagnose infectious diseases.
- Routine examination of blood, urine, feces, and cerebrospinal fluid samples by Roche automatic biochemical analyzers.

PROFESSIONAL SKILLS

- ✓ **Protein Crystallization:** Crystal Phoenix protein crystallization robot (Art Robbins Instruments) Screening; Crystal growth condition optimization with sitting drops/hangover drops.
- ✓ **Single Crystal X-ray diffraction experiment:** Picking protein crystals; Processing X-ray diffraction data from crystals; Crystal structures refinement by Phenix.
- ✓ **Surface Plasmon Resonance (SPR, GE.):** CM5/CM7/SA chips; IFC replacement.
- ✓ **GE FPLC Columns:** Size Exclusion/ Affinity/ Ion exchange chromatography.
- ✓ **Protein Expression:** Mammalian cells (CHO, adherent, and suspension 293T cells); *E. coli*.
- ✓ **Protein Refolding and Purification:** GE ÄKTA pure protein purification system (FPLC); Tangential flow filtration (TFF).

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- ✓ **Crosslinking immunoprecipitation:** BS^3/EDC/DSS/Sulfo-SMCC.
- ✓ **DNA and RNA Extraction and Identification:** Human blood; Cell culture medium; Insect tissue.
- ✓ ***In-vitro* Culture:** *Plasmodium;* Common human microorganisms; Mammalian cells; *E. coli*.
- ✓ **Polymerase Chain Reaction (PCR):** Routine PCR; Quantitative PCR.
- ✓ **Enzyme Activity:** Km, Vmax, Ki, K-on, K-off determination by Colorimetric/ Luminescent/ Fluorescent methods.
- ✓ **High Throughput Screening:** Multidrop Combi Reagent Dispenser, Echo Liquid Handlers, CyBio Felix, TEMPEST ® Liquid Dispenser, Artemis Intelligence Platform, and other robotic droplet arm equipment.
- ✓ **Other Skills:** Western blot; SDS-PAGE; Enzyme-linked immunosorbent assay (ELISA); Alpha assay; UV/VIS spectrophotometer, circular dichroism (CD), analytical ultracentrifugation (AUC); Enzyme kinetics derivation; Isothermal titration calorimetry (ITC, Microcal iTC-200); Nuclear magnetic resonance (NMR)

MAIN PROFESSIONAL COMPUTATIONAL SKILLS

- ✓ **GraphPad Prism** (GraphPad Software Inc., La Jolla, CA, USA)
- ✓ **IBM SPSS Statistics** (SPSS Inc., Chicago, IL, USA)
- ✓ **PyMOL** (Schrödinger, Inc., NY, USA)
- ✓ **Phenix** (Python-based Hierarchical ENvironment for Integrated Xtallography)
- ✓ **Coot** (Crystallographic Object-Oriented Toolkit)
- ✓ **Instant JChem** (Plexus Connect), including DARE
- ✓ **ATLAS** (Workstation), including Dotmatics
- ✓ **TIBCO Spotfire** (Cloud Software Group, Inc., Somerville, MA, USA.)
- ✓ **Computer Programming** (C Language)
- ✓ **DNAstar Lasergene** (DNASTAR Inc., Madison, WI, USA)
- ✓ **Primer Premier** (Premier Inc., Canada)

EDUCATION BACKGROUND

Ph.D. in Biochemistry and Molecular Biophysics Kansas State University Manhattan, KS

Supervisor: Dr. Brian Geisbrecht (Distinguished Professor)

Awards: College of Arts and Sciences Research Travel Award, 2021.
College of Arts and Sciences Research Travel Award, 2020.
Excellence in Biochemistry and Molecular Biophysics GRA Award, 2020-2021.

Leadership: Spring 2020 Graduate Student Leadership Development Program

Master of Medicine in Pathogenic Biology Kunming Medical University Yunnan, China

Supervisor: Dr. Zhaoqing Yang (Professor)

Awards: Outstanding Master's Dissertation in 2016.
Scholarship in the academic year of 2015-2016.

Bachelor of Medicine in Medical Examination Hebei Medical University Hebei, China

Award: Excellent Student Leader in the academic year of 2009-2010.

Leadership: President of Student News Agency of the College, 2010-2011.
Vice president of the Student News Agency of the College, 2009-2010.

SELECTED PUBLICATIONS

1. ***Xu, X.,*** Marffy, A. L. L., Keightley, A., McCarthy, A. J., & Geisbrecht, B. V. (2022). Group B *Streptococcus* Surface Protein β: Structural Characterization of a Complement Factor H–Binding Motif and Its Contribution to Immune Evasion. The Journal of Immunology. (*Top Reads of the issue, released structure PDB ID: 7S0R*).
2. ***Xu, X.,*** Zhang, C., Denton, D. T., O'Connell, D., Drolet, D. W., & Geisbrecht, B. V. (2021). Inhibition of the Complement Alternative Pathway by Chemically Modified DNA Aptamers That Bind with Picomolar Affinity to Factor B. The Journal of Immunology, 206(4), 861-873. (*Cover and Top Reads of the issue, released structures PDB ID: 7JTQ, 7JTN*).
3. ***Xu, X.,*** van Sorge, N., van der Lans, S., van Woudenbergh, E., van Strijp, J., McCarthy, A. J., & Geisbrecht, B. (2020). Structural and Interaction Insight in *Streptococcal* beta C Proteins. The FASEB Journal, 34(S1), 1-1.

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4. ***Xu, X***., Zhou, G., Wang, Y., Hu, Y., Ruan, Y., Fan, Q., ... & Cui, L. (2016). Microgeographic heterogeneity of border malaria during elimination phase, Yunnan Province, China, 2011-2013. Emerging infectious diseases, 22(8), 1363.
5. Ramyar, K. X., ***Xu, X***., White, N. M., Keightley, A., & Geisbrecht, B. V. (2019). Expression, purification, and characterization of a human complement component C3 analog that lacks the C-terminal C345c domain. Journal of Immunological Methods, *473*, 112633. (*Co-first author*).

Please see Google Scholar for more publications: https://scholar.google.com/citations?user=31CXA8YAAAAJ&hl=en

REVIEWER FOR SCIENTIFIC JOURNALS

1. Microorganisms (IF 4.5)
2. Omega ACS (IF 4.1)
3. Brain Sciences (IF 3.3)
4. Chemical Biology & Drug Design (IF 3.0)
5. Applied Science (IF 2.8)
6. Electronics (IF 2.7)

MAIN RESEARCH EXPERIENCES

Design, validation, execution, and interpretation of biochemical and biophysical assays for lead discovery, molecular profiling, and lead optimization, in support of the BMS portfolio. 2022-Present

- Theoretical and practical application of highly specialized knowledge in biophysics, *in vitro* pharmacology, and biochemical assays for studying protein-protein interactions and mechanism of action profiling of novel ligands.
- Designed biochemical experiments for drug targets including Acetylglucosaminyltransferase / Ubiquitin-specific peptidase / Tyrosine-protein phosphatase.
- Refined and validated biochemical experiments on the feasibility of HTS for drug targets including Acetylglucosaminyltransferase / Ubiquitin-specific peptidase / Tyrosine-protein phosphatase.
- Worked on cross-functional drug discovery teams, closely interacting with colleagues from different functions including chemistry, biology, biotherapeutics, and pharmacology.
- Collaborate within LDO and across project teams to help shape the *in vitro* screening strategy, identify appropriate assay platforms, and develop high throughput assays.
- Promoted all my projects forward from Pre GTS to GTS.

Structural and kinetics study of Group B *Streptococcus β* protein. 2018-2021

a) Defined the Human Complement Component Factor H (fH) binding site on β protein using a combination of structural and functional analysis: (Released structure PDB ID 7S0R)

- Expressed and purified recombinant fH and β protein and their fragments by 293T cells and *E.coli*.
- A protease-stable fragment of β protein was identified, corresponding to residues 688-789 that retained high-affinity fH binding activity by SPR assay.
- The crystal structure of this fragment was solved and refined to 2.36 Å limiting resolution, which revealed three alpha-helix bundle fold, variations of which are common among bacterial immune evasion proteins.
- A site-directed mutagenesis was performed by substituting the loop amino acids QHLQKKN to a GGGG linker on β protein were made, which significantly impaired in their ability to bind immobilized fH in an SPR assay.

b) Interaction Study of Paired Immune Receptors and GBS β-Antigen C Protein:

- To define the binding site of β protein on the leukocyte Ig-like receptors (LILRs), truncations of β protein binding to LILRs were assessed by SPR.

Structure Studies of Aptamers that Inhibit Complement Molecule Factor B. 2020

- Built and refined crystal structure models of a family of Slow Off-rate Modified DNA Aptamers (SOMAmers) that bind to human complement factor B, with a resolution at 3.1 and 3.4 Å by Phenix and Pymol. (*Released structures PDB ID: 7JTQ, 7JTN)*

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Structural and kinetics study of human complement molecules C3 and C1s. 2017-2021

a) Identification of C1s-binding with Small Molecules and Complement Inhibition Properties:

- Expressed, refolded, and purified human complement C1s protein and its truncation form by *E.coli*.
- Investigated the inhibition properties Ki, Km, and Vmax of C1s with computational molecular docking screened chemicals: Out of the 96 candidate small molecules, 17 exhibit dose-dependent, selective binding to C1s by SPR, 8 exhibit C1s inhibition properties in an enzyme activity assay, and 17 exhibit C1s inhibition properties in a hemolysis activity assay.
- Screened and optimized the crystallization conditions to obtain protein crystals for X-ray diffraction analysis.

b) Expression, purification, and characterization of a human complement component C3 analog that lacks the C-terminal C345c domain.

- Expressed and purified human complement C3 analog with CHO cells.
- Detect the protein dimerization in solution by AUC.

Identification of the epidemiology of mixed infection of *Plasmodium* and helminths. 2015-2016

- Collected feces and blood samples from 3 elementary schools in the China-Myanmar border area.
- 1300 feces samples were tested by the Kato Katz method to determine the type of helminth eggs and have them counted.
- The same number of blood samples were used for *plasmodium* type identification by PCR, glucose-6-phosphate dehydrogenase (G6PD) deficiency determination by fluorescence spot method, and routine blood test by flow cytometry.

***Plasmodium vivax in vitro* cultivation and drug resistance gene determination on-site.** 2014-2015

- Cultivation of *Plasmodium vivax* patients' blood samples *in vitro* with human-type O red blood cells.
- On-site *in vitro Plasmodium vivax* drug resistance gene determination of *Pvmdrl, Pvcrt-o, Pvdhfr, and Pvdhps* in the China-Myanmar border area.

***Plasmodium falciparum in vitro* culture and drug resistance gene determination.** 2013-2014

- Cultivation of *Plasmodium falciparum* patients' blood samples *in vitro*.
- *In vitro Plasmodium falciparum* drug resistance gene determination*: Pfmdr1, Pfmcrt, and Pfdhps.*