Chenglong Li
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OBJECTIVE

A challenging academic faculty or principal investigator position in areas of computational biochemistry and structural biology.

PROFESSIONAL SKILLS

1) Molecular modeling (Monte Carlo simulation, molecular dynamics simulation, SA/GA/EA optimization, molecular mechanics, quantum chemistry, conformational analysis, homology modeling and threading); [programs: AMBER, CHARMM, Discover, MacroModel, DelPhi, MOE, CaChe, Gaussian, MOPAC, MODELLER, etc]

2) Structure-based drug design (molecular docking, virtual library screening (vHTS), lead derivation, *de novo* ligand design, QSAR, transition-state analog design based on enzyme mechanistic studies); [programs: AutoDock, Ludi, etc]

3) Protein X-ray crystallography (proteins and their complexes with various ligands); [programs: HKL(Denzo/Scalepack), Mosflm, SnB, Solve, SHELX, Amore, MLphare, SHARP, ARP/wARP, CCP4, PHASES, O, CHAIN, X-PLOR, CNS, etc]

4) Computational programming and scripting (primarily on UNIX/LINUX-based platforms, With experience on both workstations and parallel supercomputing/cluster computing with Fortran, C, Python and Perl languages);

5) Thermal and thermodynamic analysis (DSC and ITC, etc);

6) Photochemical analysis (“matrix isolation”, etc);

7) Surface analysis (ESCA(XPS/UVPS), adsorption, etc);

8) Fluency in both English and Chinese (oral and written).

EDUCATION

Ph.D. in Biochemistry and Biophysics, Cornell University, Jan. 2000.

M.Sc. in Physical Chemistry, Peking (Beijing) University, China, July 1988.

B.Sc. in Chemistry, Peking (Beijing) University, China, July 1985.

EXPERIENCE

The Scripps Research Institute

May 2002 – present. Senior research associate in computational chemistry and biology.

Structure-based drug design on AICAR/GAR transformylases and GPCRs:
1) Drug lead searching via virtual library screening;
2) Lead optimizations and derivations;
3) Transition state analog design;
4) Inhibitor design via fragment-tethering;
5) Free energy simulations;
6) Homology modeling of GPR41, GPR43;
7) Protein-protein docking of Siah/SIP in the ubiquitin-mediated proteasomal protein degradation.

The Burnham Institute

July 2000 – May 2002. Postdoc in molecular modeling and structural analysis.

Three major projects:
1) Structural modeling of RIZ PR tumor suppressor domain;
a) PR structural modeling and prediction; b) PR crystallization and X-ray structural determination.
2) TRAF3 *apo* structure, TRAF3/peptide complexes and ligand design. (TRAF3 is an important regulatory protein in signal transduction cascades and apoptosis).
3) Structure-based/computer-aided drug design against caspase 3.

Cornell University

January 1994 – January 2000. Ph.D. candidate in Biochemistry and Biophysics.

Research assistant. Projects include:
1) High resolution structure of *E. coli* PNP (purine nucleoside phosphorylase);
2) "Suicide" Gene Therapy; Structure-based pro-drug design using *E. coli* PNP as the foreign gene weapon;
3) Three-dimensional structure determination of AIR (aminoimidazole ribonucleotide) synthetase in the *de novo* purine nucleotide biosynthetic pathway, and its mechanistic studies.

Teaching Assistant (August 1993 – December 1993). Assignment includes:
Organic Chemistry tutoring; Experiment implementing and lab report evaluating; Exam proctoring and grading.

Auburn University

January 1991 - July 1993. Research associate in Physical Organic Chemistry.

Projects include:
1) Studies on trans-cycloheptene by means of matrix-isolation and molecular mechanics; This is the most strained double bond to date, a reactive intermediate;
2) Photochemical studies on dienes; Potential energy surfaces of butadienes on cyclobutene formation and double bond isomerization;
3) Studies on the reactive intermediate diimide, a stereoselective hydrogenation agent; The elusive cis-diimide has been trapped by us.

Huadi (China Geochemical) Corporation

July 1989 - September 1990. Research Scientist.

Project: Research on raising petroleum extraction efficiency.

Institute of Biophysics, Academia Sinica

August 1988 - June 1989. Research associate.

Projects include:
1) Setup of a new DSC (differential scanning calorimetry) lab for protein conformational studies;
2) Conformational and energetic studies on Na^+, K^+ - ATPase reconstituted in liposomes, and its interaction with lipids and drugs like anisodamine, etc.

Peking (Beijing) University

July 1985 - July 1988. M.Sc. Graduate student in physical chemistry.

Projects include:
1) Interaction between polymers and surface-active agents in solutions and solid/liquid interfaces;
2) Surface properties of aqueous gels.

PUBLIC SERVICE

1994-1995, Executive member in charge of Public Relation, the Chinese Students and Scholars Associations at Cornell.

March 1989 - December 1989, Science and technology news translator, *China Science and Technology Daily*.

Summer 1986, Technology consultant on small business development for the China Twilight Project.

1984 – 1985, Member, Peking University Sciences club.

HONORS

US Department of Defense Army breast cancer Fellowship (2001-2004).

Outstanding Graduate Student in Research (1988), Peking University.

3rd Award in Encyclopedic Knowledge Competition (1982), Peking University.

The 1st Class Award in Mathematics Competition in China (1981), Anhui Elite Senior High School.

PUBLICATIONS (research highlights in parenthesis)

Manuscript in preparation

Chenglong Li and Arthur J. Olson. "A Binding Free Energy Simulation of Avian IMP Cyclohydrolase in Complex with a Sulfonyl-containing Transition-state Nucleoside Analog". ***J. Am. Chem. Soc.***
(A MM-PBSA combined molecular dynamics and Poisson-Boltzmann solvation free energy method revealed that the enzyme internal vibrations enhances the binding of transition-state analog entropically, consistent with higher crystallographic B-values of the *holo*-complex than the *apo*-enzyme. It raises the interesting question about the dynamic contribution of enzyme to transition-state stabilization during the enzymatic catalysis, and has implications on the transition-state analog design.**)**

Chenglong Li and Arthur J. Olson. "A Comparative Docking Study of Substrate, Transition-state and Product against Human IMP Cyclohydrolase *apo*- and *holo*-sites". ***J. Am. Chem. Soc.***

Brikanarova, K., Nasertorabi, F., Havert, M.L., Eggleston, E., Hoyt, D.W., Li, C., Olson, A.J., Vuori, K. and Ely, K.R. "The Serine-Rich Domain from Crk-Associated Substrate (p130Cas) is a Four Helix Bundle". ***Proc. Natl. Acad. Sci. USA***

Santelli, E., Li, C., Olson, A. J., Reed, J. C., Liddington, R., Ely, K. R. and Matsuzawa, S.-I. "Structural and Functional Study on the Siah/SIP complex in the Proteasome-mediated Proteolysis". ***Cell.***
(A combined crystallographic, protein-protein docking, NMR and bio-functional study on the interaction between Siah (an E3 ligase) and SIP (an important regulatory protein linking E3 enzyme with SCF box) in the protein ubiquitination process. The homodimer of SIP N-term domain concave "hooks" with the Siah homodimer concave with their 2-fold axis coincide each other. The critical conserved peptide motif PxAxVxP of SIP "tags" to the

edge of Siah β-sheet, reminiscent of TRAF3/TANK interaction. The latter is especially interesting because Siah and TRAF proteins share the same β-sandwich topology.**)**

Papers published

Chenglong Li, Lan Xu, Dennis W. Wolan, Ian A. Wilson and Arthur J. Olson. "Virtual Screening of Human AICAR Transformylase against the NCI Diversity set Using AutoDock to Identify Novel Non-folate Inhibitors". ***J. Med. Chem***., in press.
(We developed a highly successful virtual screening protocol to search novel leads with AutoDock. The hierachical screening has two-stages: the first stage diversity library docking, and the second stage combining ligand similarity searching and docking selection. The computational protocol is highly modular and customizable.**)**

Lan Xu, Chenglong Li, Arthur J. Olson and Ian A. Wilson. "Crystal Structure of Avian AICAR Transformylase in Complex with a Novel Inhibitor Identified by Virtual Ligand Screening". ***J. Biol. Chem***., in press.

Chenglong Li, Paula S. Norris, Chao-Zhou Ni, Marnie L. Havert, Elizabeth M. Chiong, Bonnie R. Tran, Edelmira Cabezas, John C. Reed, Arnold C. Satterthwait, Carl F. Ware, and Kathryn R. Ely. "Structurally Distinct Recognition Motifs in Lymphotoxin-β Receptor and CD40 for Tumor Necrosis Factor Receptor-associated Factor (TRAF)-mediated Signaling". ***J. Biol. Chem***., Dec 2003; **278**: 50523 - 50529.

Eric M. Bennett, Chenglong Li, Paula W. Allen, William B. Parker, Steven E. Ealick. "Structural Basis for Substrate Specificity of *Escherichia coli* Purine Nucleoside Phosphorylase", ***J. Biol. Chem***., 2003, **278**: 47110-47118.
(This is an *E. coli* purine nucleoside phosphorylase based "suicide" gene therapy project. We are trying to design 6-amino-purine nucleoside analogues as better pro-drugs to trigger the foreign gene weapon for cancer cell "bystander" killing. Both enzyme and ligand can be manipulated for a better "lock-and-key" combination. Particularly for the ligand, both purine base and ribose parts can be modified for "smoother" glycosidic bond-breaking. Combined X-ray crystallography and molecular modeling have been utilized.**)**

Yan Zhang, Joel Desharnais, Thomas H. Marsilje, Chenglong Li, Michael P. Hedrick, Lata T. Gooljarsingh, Ali Tavassoli, Stephen J. Benkovic, Arthur J. Olson, Dale L. Boger, and Ian A. Wilson. "Rational Design, Synthesis, Evaluation and Crystal Structure of a Potent Inhibitor of Human GAR Tfase: 10-Trifluoroacetyl-5, 10-Dideaza-Acyclic-5, 6,7,8-Tetrahydrofolic acid". ***Biochemistry***, 2003, ***42*****(20)**: 6043-6056.
(This paper describes the most potent and specific GAR transformylase inhibitor to date. A comparative docking study of native folate cofactor to different enzyme conformations identifies the most transition-state like GAR transformylase template which offers an excellent platform for our continuing structure-based inhibitor design.**)**

Ni CZ, Li C, Wu JC, Spada AP, Ely KR. "Conformational restrictions in the active site of unliganded human caspase-3", ***J. Mol. Recognit***. 2003 May-Jun, **16(3)**:121-4.

Shu-ichi Matsuzawa, Chenglong Li, Chao-Zhou Ni, Shinichi Takayama, John C. Reed, and Kathryn R. Ely. “Structural Analysis of Siah1 and Its Interactions with Siah-interacting Protein (SIP)”. ***J. Biol. Chem***., Jan 2003; **278**: 1837 - 1840.

Kathryn R. Ely, Chenglong Li. “Structurally Adaptive Hot Spots at a Protein Interaction Interface on TRAF3”, ***J. Mol. Recognit***., Nov. 2002, **15**(5), 286-290.

Chenglong Li, Marnie L. Havert, Edelmira Cabezas, Arnold C. Satterthwait, Chao-Zhou Ni, Jeannie He, John C. Reed, Genhong Cheng, Kathryn R. Ely. “Downstream Regulator TANK binds to the CD40 Recognition Site on TRAF3”, ***Structure***, March 2002, **10**: 403-411.
(We have discovered a secondary protein β-strand motif binding site of TRAF3 besides the primary binding cleft. This may have important implication on understanding the general TRAF/protein signal transduction cascade in many processes including NF-κB and JNK activations. It may also facilitate the inhibitor design against TRAF6 because of their topological similarities.**)**

Li C, Kappock TJ, Stubbe J, Weaver TM, and Ealick SE. "X-ray Crystal Structure of Aminoimidazole Ribonucleotide Synthetase (PurM) from the *Escherichia coli* Purine Biosynthetic Pathway at 2.5Å Resolution", ***Structure***, September 1999, **7**: 1155-1166.
(We used Baysian data filtering and MAD phasing to solve the largest Selenium substructure at that time. A combined multi-resolution density matrix averaging had to be used to reveal the chain connectivity. A novel ATP binding motif was discovered.**)**

Mueller EJ, Oh S, Kavalerchik E, Kappock TJ, Meyer E, Li C, Ealick SE, and Stubbe J. “Investigation of the ATP Binding Site of *Escherichia coli* Aminoimidazole Ribonucleotide Synthetase Using Affinity Labeling and Site-Directed Mutagenesis”, ***Biochemistry***, 1999, **38**: 9831-9839.

Chenglong Li, Feng Huang. "Effect of Anisodamine on Activity of Na^+, K^+ - ATPase Reconstituted in Several Liposomes", The 1st National Molecular Biophysics Conference held in Xiamen in 1989.

Li, C., Ma, C.-M.. "Stability of Dispersions of Iron Oxide in Mixed Solutions of Polyvinylpyrrolidone and Sodium Alkyl Sulfates", ***Colloids and Surfaces*** (Elsevier), 1990, **47**: 117-23.

Li, C., Ma, C.-M.. "Interaction Between Polyvinylpyrrolidone and Sodium Dodecyl Sulfate at Solid/liquid Interfaces", ***J. Colloid and Interface Sci.*** **(USA)**, 1989, **131**(2): 185-92.

Chenglong Li, Di Qiang. "Surface Properties of Aqueous Gels", The 3rd National Colloid and Surface Sciences Conference held in Shanghai in 1986.

ACADEMIC JOURNAL REVIEWER

Journal of The American Chemistry Society
Journal of Medicinal Chemistry
Proteins: Structure, Function, and Bioinformatics
Bioorganic and Medicinal Chemistry Letters
Journal of Computer-Aided Molecular Design

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