This supplement is intended to focus on ligand-receptor interactions and drug design. Biochemistry of ligand binding, experimental drug design and computational drug design are included within the supplement’s scope.

Biochemistry Insights aims to provide researchers working in this complex, quickly developing field with online, open access to highly relevant scholarly articles by leading international researchers. In a field where the literature is ever-expanding, researchers increasingly need access to up-to-date, high quality scholarly articles on areas of specific contemporary interest. This supplement aims to address this by presenting high-quality articles that allow readers to distinguish the signal from the noise. The editor in chief hopes that through this effort, practitioners and researchers will be aided in finding answers to some of the most complex and pressing issues of our time.

Articles should focus on ligand-receptor interactions and drug design and may include the following topics:

- **Biochemistry of ligand binding**
  - Amphiphilic drugs, binding mechanism, binding modes, binding properties, bispecific ligands, drug targets, drug-drug interactions, electrostatic interactions, endocrine receptors, hydrogen bonding, hydrophobic interactions, intermolecular interactions, ligand activation, ligand binding affinity, ligand conformers, ligand specificity, ligand-directed signaling, ligand-protein conjugates, ligand-selective activity, ligand-specific binding, lipophilicity, molecular conservation, molecular recognition, multi-mode ligand-receptor interactions, molecular scaffolds, multiple ligand recognition, multivalent ligand-receptor interactions, nuclear receptor ligands, nuclear receptors, polar contacts, receptor inhibition, quantum chemical-based drug-receptor interaction, receptor modulators, structural conservation, target-ligand interface, universal ligand.

- **Experimental drug design**
  - Affinity purification, apoptosis-mediating receptor-ligand systems, clinical pharmacokinetics, cofactor discovery, differential mass spectrometry, differential scanning fluorimetry, drug screening, fluorescence interference detection, fluorescent ligand, high-throughput assays, in vivo chemical crosslinking, live zebra-fish-based screening system, mutational analysis, myocardial perfusion imaging, plant-derived ligands, radiolabeled ligand interactions, receptor imaging, spectrometry, time resolved FRET strategy.

- **Computational drug design**
  - Chemocentric informatics approach, computational modeling, computer-assisted design, evolutionary design of ligands, in silico approaches, knowledge-based scoring functions, molecular docking, prediction of ligand binding, prediction of ligand-induced structural polymorphism, quantitative structure-activity relationships, rational approach to drug design, rationally designed mutations, structure-guided drug design, structure-based design, virtual screening.

At the discretion of the guest editors other articles on other relevant topics within the scope of the supplement may be included.
Protein receptors are utilized by all living organisms to sense the environment and monitor internal physiological states. By binding with ligands, receptors activate or inhibit downstream biochemical signaling pathways to make adjustments in cellular processes (gene expression profile, metabolic flow, etc.). Dysfunction of these signaling pathways is responsible for various human diseases like cancer, diabetes and so on. Receptor signaling can be improperly over-activated (e.g. BCR-ABL oncogene in chronic myeloid leukemia), or impaired as a result of either lacking the ligand or mutations in the receptor complex (e.g. type I and II diabetes). Therefore, receptors are the targets of a lot of pharmaceutical agents. The study of receptors and their ligands is critical for elucidating the physiological and pathological processes they are involved in. By understanding the underlying mechanisms, we can find better ways to improve human health.

In this issue, three studies about ligand-receptor interaction are presented. Various aspects of the drug discovery dynamics are covered: how to prepare ligands in vitro, how to study functional receptors in vivo and how we can rationally design drugs based on what we know about ligand-receptor interactions. All of them are aimed for clinical applications.

In Wu et al, a novel way for preparing a promising drug candidate Olesoxime (cholest-4-en-3-one) is described. Olesoxime has been reported to bind two proteins of the mitochondrial permeability transition pore: the voltage-dependent anion channel and the peripheral benzodiazepine receptor.

Wu et al set out to prepare this ligand in a defined, cell extract-free procedure and successfully acquired a product with a purity of 99.78%. With its analgesic and neuroprotective effect, olesoxime is a promising compound for treating multiple neuropathies: amyotrophic lateral sclerosis (ALS), Huntington disease, Parkinson disease, and even autism. Although a recent Phase II/III with ALS patients did not show conclusive benefits, other clinical trials with muscular dystrophy patients have been gaining momentum.

In Jin’s study, the molecular mechanism of an important phenomenon, cold pain, is probed with receptor/ligand interaction. Most of us are familiar with the nocuous headache when our dental pulp is exposed to cold drink/food. It is already known that transient receptor potential (TRP) channels are little antennas responsible for our sensations to temperature, pressure, taste, vision and pain. The cold pain pathway is less understood than other sensations but generally thought to be mediated by TRP channels. While only in vitro or behavioral approaches have been used previously, Dr. Jin took a functional approach to tackle this problem, modifying the status of TRP channels with a broad spectrum TRP channel blocker to show that this can suppress the response of nociceptive neurons to cold stimulation in dental pulp.

Moreover, this study showed for the first time that in vivo electrophysiological technique can be used as an alternative and effective approach for evaluating the effects of some drugs in animal models. It could open up new therapeutic routes for an age old problem.

Finally, an excellent review by Dr. Chen describes carbamoylated EPO, a derivative of natural Erythropoietin (EPO). EPO is widely known for its role in red blood cell production (erythropoiesis). It is medically used in various anaemia conditions and, unfortunately, consumed by some athletes illegally for performance enhancing. In addition, EPO also has a non-classical role in neuro-protection. The dual roles of EPO are mediated by different receptor complexes. This presents an opportunity to design EPO derivatives that are neuro-protective but not erythropoietic in order to avoid side effects resulting from high dose EPO usage, like thrombosis. Carbamoylated EPO is one of such derivatives. This is an elegant case of rational drug design at its finest using ligand receptor biology.

In summary, we hope this issue on Ligand-Receptor Interactions and Drug Design gives you more thoughts on the diversity and great potential of this topic. More exciting findings are on the way.

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Lead Guest Editor Dr. Yanling Zhang

Dr. Yanling Zhang is an assistant professor in the Department of Biochemistry and Molecular Biology at Soochow University, China. He completed his PhD at the University of Iowa and has previously worked at the University of Michigan. He now works primarily in membrane trafficking and neurodegenerative diseases. Dr. Zhang has published a number of papers in prestigious journals including Nature, PNAS and EMBO Journal. Dr Zhang can be contacted at yanlzhan@suda.edu.cn.

Guest Editors

DR. JIANRUI SONG
Dr. Jianrui Song is a PhD Candidate at the Department of Cell and Developmental Biology at University of Michigan. She completed her Master degree at The Second Military Medical University in Shanghai. Her work spans autophagy, cancer and cardiovascular disease. Dr. Song is the author or co-author of 15 published papers. She can be contacted at jruisong@umich.edu.

DR. XIAOJUN ZHANG
Dr. Xiaojun Zhang is a Research Associate at the University of Southern California. He completed his PhD at Florida State University. Dr. Zhang is the author or co-author of more than 15 published papers and has presented at multiple national conferences. He specializes in biophysics. Dr Zhang can be contacted at xiaojunz@usc.edu.

DR. YUANYUAN XIAO
Dr. Yuanyuan Xiao is a research scientist in the Department of Internal Medicine at the University of Michigan. She completed her PhD at the Institute of Biochemistry and Cell Biology in Shanghai and has previously worked in the Life Sciences Institute at the University of Michigan. She is an expert in metabolic diseases. Dr Xiao can be contacted at yyxiao@umich.edu.

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CORRESPONDENCE: yanlzhan@suda.edu.cn

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