**Department of Chemistry**

**Seminar** On

*Drug Discovery & Biomedical Sciences**


## Dr. Jin Wang

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BS, Peking University, China, 2003

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https://www.bcm.edu/research/labs/jin-wang


# Bridging Chemistry and Biology for New Classes of Imaging Probes and Therapeutic Drugs

The overarching goal for my research is to develop new tools for advancing biological research and new therapies for improving human health at the interface of chemistry and biology. My group has made major contributions in the areas of ratiometric redox probes and small molecule drugs. Glutathione (GSH) is the most abundant non-protein thiol in eukaryotic cells. Together with its oxidized partner (GSSG), GSH maintains cellular redox homeostasis, regulates protein functions through *S*-glutathionylation, and acts as a signaling molecule to directly activate gene expression. Currently, the concentration of intracellular GSH is derived from either cell lysates or GSH-*S*-transferase (GST) dependent probes. These approaches, however, cannot provide information about the real-time dynamics of GSH concentration changes. We developed a fluorescent probe that can reversibly react with GSH and quantitatively monitor the real-time GSH dynamics in living cells for the first time. This new GSH probe enables unprecedented opportunities to study GSH spatiotemporal dynamics, which will revolutionize our understanding of its physiological and pathological roles in living cells. On the other hand, we also developed a small molecule inhibitor of steroid receptor coactivator-3 (SRC-3) as a novel targeted cancer therapy. The Holy Grail of drug discovery is to render small molecules the power of biologics to regulate protein-protein interactions. SRC-3 is a large, non-structured nuclear protein which regulates many signaling pathways that are essential for tumor formation. Through high throughput screening and medicinal chemistry optimization, we identified SI-2 that can direct interact with SRC-3 and selectively reduce its transcriptional activities and protein concentrations, leading to selective induction of breast cancer cell death with a low nM $IC_{50}$ value, and inhibition of primary tumor growth in a breast cancer mouse model. This work will not only potentially improve breast cancer treatment through the development of a 'first-in-class' drug that targets oncogenic coactivators, but also encourage other researchers to develop strategies to target protein-protein interactions that are designated as 'important but undruggable' targets in the future.

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| DATE: | Friday, October 27, 2017 | |
| TIME: | 4:00 – 5:00 pm | *Coffee, donuts and gathering at 3:45 pm* |
| LOCATION: | CCSB G.0208 | *The seminar auditorium below Starbucks* |
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