

北京大学基础医学院

院长论坛

报告题目: Cellular Biochemical Activity Architecture for Signal Sensing and Processing

报告人: Jin Zhang, Ph.D.

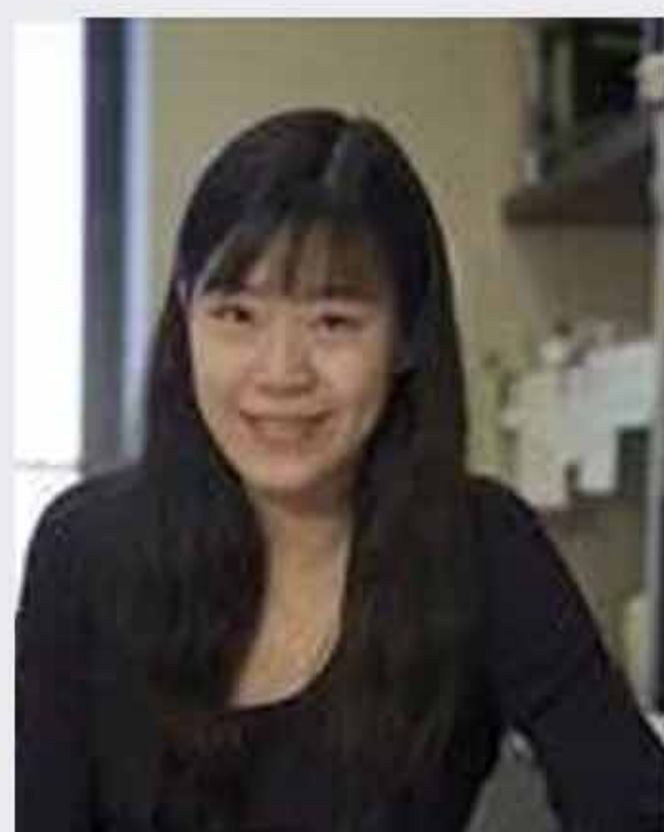
University of California, San Diego

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地点: 北京大学医学部生化楼三层中厅

主持人: 张勇 研究员

报告人简介:



Intracellular signaling pathways in the brain play a central role in regulating neuronal activity and synaptic plasticity. We have developed a series of fluorescent biosensors to probe the spatiotemporal regulation of signaling molecules, such as protein kinases, phosphatases and second messengers, in living systems. In this talk, I will discuss some of the imaging technologies; and focus on cAMP/PKA and calcium signaling pathways and present studies where we combined genetically encoded fluorescent biosensors, superresolution imaging, targeted biochemical perturbations and mathematical modeling to probe the biochemical activity architecture of the cell.

Representative Publications:

- DiPilato LM, Cheng X, and **Zhang J**. Fluorescent Indicators of cAMP and Epac Activation Reveal Differential Dynamics of cAMP Signaling within Discrete Subcellular Compartments. *Proc. Natl. Acad. Sci. USA* 2004; 101: 16513-16518.
- Zhou X, Clister TL, Lowry PR, Seldin MM, Wong GW and **Zhang J**. Dynamic Visualization of mTORC1 Activity in Living Cells. *Cell Rep*. 2015, 10(10): 1767-1777. PMID: PMC4567530
- Ross BL, Tenner B, Markwardt ML, Zviman A, Shi G, Kerr JP, McFarland JJ, Mauban JR, Ward CW, Rizzo MA† and Zhang J†. Single-Color, Ratiometric Biosensors for Detecting Signaling Activities. †Co-corresponding authors. *eLife*. 2018, 7: e35458.
- Mehta S†*, Zhang Y*, Roth RH*, Zhang J†, Mo A, Tenner B, Haganir RL†, and **Zhang J**†. A Suite of Single-fluorophore Biosensors for Sensitive and Multiplexed Detection of Signaling Activities. *Equal contribution. †Co-corresponding authors. *Nat. Cell Biol*. 2018, 20(10):1215-1225.
- Sample V*, DiPilato LM*, Yang J*, Ni Q†, Saucerman JJ† and **Zhang J**†. Regulation of Nuclear PKA revealed by spatiotemporal manipulation of cAMP. *Equal contribution. †Co-corresponding authors. *Nature Chem. Biol*. 2012; 8(4): 375-82. PMID: PMC3307945
Summary: We developed a new method of using bicarbonate-activatable and genetically targetable soluble adenylyl cyclase to control the location, kinetics and magnitude of the cAMP signal. Using this method in conjunction with fluorescence imaging and mechanistic modeling, we uncovered the activation of a resident pool of PKA holoenzyme in the nuclei of HEK-293 cells, modifying the existing dogma of nuclear cAMP-PKA signaling.
- Sample V, Ni Q, Mehta S, Inoue T, **Zhang J**. Controlling Enzymatic Action in Living Cells with a Kinase-Inducible Bimolecular Switch. *ACS Chem. Biol*. 2013; 8(1): 116-21. PMID: PMC3549020
- Miyamoto T†, Rho E, Sample V, Akano H, Magari M, Ueno T, Gorshkov K, Chen M, Tokumitsu H, **Zhang J**†, and Inoue T†. Compartmentalized AMPK signaling illuminated by genetically encoded molecular sensors and actuators. †Co-corresponding authors. *Cell Rep*. 2015, 11(4):657-70. PMID: PMC4417068
- Dedecker P†, Mo GCH, Dertinger T, and **Zhang J**†. Widely accessible method for superresolution fluorescence imaging of living systems. †Co-corresponding authors. *Proc. Natl. Acad. Sci. USA* 2012; 109(27): 10909-14. PMID: PMC3390831
- Dedecker P, Duwé S, Neely RK, and **Zhang J**. Localizer: fast, accurate, open-source, and modular software package for superresolution microscopy. *J. Biomed. Opt*. 2012; 17(12): 126008. PMID: PMC3512108
- Hertel F, Mo GCH, Duwé S, Dedecker P, and **Zhang J**. RefSOFI for Mapping Nanoscale Organization of Protein-protein Interactions in Living cells. *Cell Rep*. 2016, 14(2):390-400. PMID: PMC4870019
- Mo GCH, Ross B, Hertel F, Manna P, Yang X, Greenwald E, Booth C, Plummer AM, Tenner B, Chen Z, Wang Y, Kennedy EJ, Cole PA, Fleming KG, Palmer A, Jimenez R, Xiao J, Dedecker P, and **Zhang J**. Genetically-Encoded Biosensors for Visualizing Live-cell Biochemical Activity at Superresolution. *Nat. Met*. 2017; 14(4): 427-434. PMID: PMC5388356
- Newman RE*, Hu J*, Rho H*, Xie Z*, Woodard C, Neiswinger J, Hwang W, Shirley M, Hu S, Cooper C, Jeong JS, Wu G, Lin J, Gao X, Ni Q, Ji H, Desiderio S, Dalby KN, Birnbaum MJ, Cole PA, Knapp S, Ryazanov A, Zack DJ, Blackshaw S, Pawson T, Gingras A, Pandey A, Turk BE, **Zhang J**†, Zhu H†, Qian J†. Construction of human activity-based phosphorylation networks. *Equal contribution. †Co-corresponding authors. *Mol. Syst. Biol*. 2013; 9:655. PMID: PMC3658267
- Hu J*, Rho HS*, Newman RH*, Hwang W, Neiswinger J, Zhu H†, **Zhang J**†, Qian J†. Global analysis of phosphorylation networks in humans. *Equal contribution. †Co-corresponding authors. *Biochim Biophys Acta*. 2013, S1570-9639(13)00122-2. PMID: PMC3815481
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- Ni Q*, Ganesan A*, Aye-Han N*, Gao X, Allen MD, Levchenko A†, and **Zhang J**†. Signaling Diversity of PKA via a Ca²⁺-cAMP-PKA Oscillatory Circuit. *Equal contribution. †Co-corresponding authors. *Nature Chem. Biol*. 2011; 7(1):34-40. PMID: PMC3073414
- Gao X, Lowry P, Zhou X, Depry C, Wei Z, Wong GW, and **Zhang J**. PI3K/Akt signaling requires spatial compartmentalization in plasma membrane microdomains. *Proc. Natl. Acad. Sci. USA* 2011; 108(35): 14509-14. PMID: PMC3167518
- Mehta S, Aye-Han N, Ganesan A, Oldach L, Gorshkov K, and **Zhang J**. Calmodulin-controlled Spatial Decoding of Oscillatory Ca²⁺ Signals by Calcineurin. *eLife*. 2014, 3: e03765. PMID: PMC4141273
- Gorshkov K, Mehta S, Ramamurthy S, Ronnett GV, Zhou F-Q, **Zhang J**. AKAP-mediated feedback control of cAMP gradients in developing hippocampal neurons. *Nature Chem. Biol*. 2017; 13(4): 425-431. PMID: PMC5362298

欢迎师生参加!

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