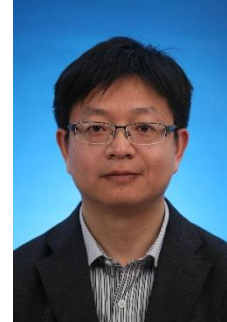


Illumination of RNA dynamics using fluorescent RNAs and optogenetic switches

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Abstract

Numerous studies show that RNAs have highly complex distributions, behaviors, and functions in cells. A robust fluorescent protein (FP)-like approach for tagging RNAs in order to monitor RNA dynamics in live cells remains to be developed. We have developed series of monomeric, highly bright, and stable fluorescent RNAs (FRs) with a broad range of emission maxima spanning from cyan to red. These FRs allow simple and robust imaging of mRNA and other RNA species in live cells with minimal perturbation of the target RNA's transcription, localization, and translation. We further show the usefulness of these FRs in imaging of genomic loci through CRISPR display, real-time tracking of protein-RNA tethering, and super-resolution imaging of RNA by structured illumination microscopy. To control intracellular RNA metabolism, we have engineered photoswitchable RNA binding proteins that binds to a specific RNA sequence in response to blue light irradiation. When fused to various RNA effectors, these optogenetic switches allow precise control of RNA localization, splicing, translation and stability in cell culture. When combined with CRISPR-Cas systems, these switches allow efficient and tunable photoswitchable regulation of transcription and genomic locus labeling. These FRs and optogenetic switches provide useful tools for investigation dynamics and functions of RNAs in live cells.

Biography

Dr. Yang holds a B. S. degree in Biological Science and Biotechnology and Ph. D. degree in Biochemistry from Tsinghua University. From 1999 to 2005, he worked as research fellow in B.L. Vallee's lab in Harvard Medical School, and then in J.L. Loscalzo's lab in Boston University School of Medicine. In 2005, he returned to Harvard Medical School as Instructor of Medicine. Dr. Yang joined the faculty of newly founded School of Pharmacy, and State Key Laboratory of Bioreactor in East China University of Science and Technology in 2006, as a Specially Appointed Professor of Biochemistry. In 2012, he won the National Outstanding Young Scientist Award in 2012. In 2014, he became the deputy director of the State Key Laboratory of Bioreactor Engineering, and established the Optogenetics & Synthetic Biology Interdisciplinary Research Center. In 2015, he was named as the Chang Jiang Scholar Distinguished Professor. In 2016, he

was named as National Young Scientific and Technological Innovation Leading Talent. In 2021, he was awarded the program to build Innovative Cluster for Cell Metabolism Monitoring and Control by National Natural Science Foundation of China.

Dr. Yang' research is focused on methodologies for fluorescence imaging and optogenetical manipulation of living cells, and their applications, including anti-cancer drug screening and bio-manufacturing. Dr. Yang has authored or co-authored more than 100 research articles, many of them published in high profile journals such as Nature Biotechnology, Nature Methods and Cell Metabolism. He also filed more than 40 international and domestic invention patents. The optogenetic technologies developed in Dr. Yang's lab are currently utilized in many research labs worldwide.