Reversible Metabolic Complexes for Novel Drug Discovery

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Sequential metabolic enzymes have long been hypothesized to form transient multienzyme complexes to regulate metabolic pathways in cells. However, it has been still challenging to monitor reversible metabolic complexes in living cells in real-time, thus making it difficult to understand underlying mechanisms of metabolic plasticity associated with human diseases. Our innovative application of fluorescence single-cell microscopy with human living cells has allowed us to discover human *de novo* purine biosynthetic complex, the "purinosome" (An et al. *Science* (2008) 320, 103-106), as the first example of this cellular phenomenon in living cells. Here, we will discuss our recent progress revealing existence of two intermediate complexes that are formed prior to complete purinosome assemblies, thus indicating a step-wise assembly mechanism of the purinosome. In addition, our quantitative biophysical evidence supports that purinosomes are indeed different cellular structures from organelles and other identified granules in human cultured cells (e.g. stress granules and cytoplasmic aggresomes). Given that purine metabolism has been a validated pharmaceutical target for chemotherapeutic agents, our research characterizing fundamental mechanisms of the purinosome (and other metabolic complexes) in living cells has great potential to be translated to treat a broad scope of human diseases associated with purine metabolism.

Biography

Dr. An has completed his PhD from the University of Minnesota, Twin Cities, and postdoctoral training from the Pennsylvania State University. He is an Assistant Professor of the University of Maryland, Baltimore County (UMBC) and he is also affiliated with the University of Maryland School of Medicine. He has published more than 13 articles and has been serving as an editorial board member of repute.