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Editorial

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New Frontiers in Kinases

In this special cross-thematic issue with *ACS Chemical Biology*, *ACS Medicinal Chemistry Letters*, and the *Journal of Medicinal Chemistry*, *Biochemistry* presents a series of papers focused on kinases. These include a study by Bastidas et al. (DOI: 10.1021/bi500684c) that provides novel mechanistic insight into product release in the PKA catalytic cycle obtained from the apo and ADP-bound crystal structures of the catalytic subunit of PKA. Additional insight into PKA is provided by Burgers et al. (DOI: 10.1021/bi500721a), who developed a bioinformatic tool, termed THAHIT, to identify novel interactions of A-kinase anchoring protein (AKAP) with PKA, some of which were experimentally validated. Rudolph et al. (DOI: 10.1021/bi501101v) characterize the properties of ERK1/2 inhibitors and find that a high-affinity, slow dissociation inhibitor stabilizes different conformations of ERK2 and reveal conformational selection toward the active kinase. Kannan et al. (DOI: 10.1021/bi501261j) have also studied kinase inhibitors with a focus on mitogen-activated protein kinase-interacting kinases (Mnks). Docking and molecular dynamics simulations suggest that the activities of some previously identified inhibitors arise from interactions with multiple active site residues. Kinase inhibitors were also studied by Leung and Shilton (DOI: 10.1021/bi500959t), although in this case, it involved the demonstration that a number of CK2 inhibitors such as 4,5,6,7-1*H*-tetrabromobenzimidazole (TBBz) and 2-dimethylamino-4,5,6,7-tetrabromo-1*H*-benzimidazole (DMAT) have off-target effects and can also bind to the active site of quinone reductase 2. Krisenko et al. (DOI: 10.1021/bi500325n) used multiharmonic atomic force microscopy to define the role of the Syk protein tyrosine kinase in the topography, elasticity, viscosity, and microtubule network in living breast cancer cells, while Wang et al. (DOI: 10.1021/bi5013113) used hydrogen−deuterium exchange mass spectrometry and nuclear magnetic resonance to define the interaction of the human pyruvate dehydrogenase complex with pyruvate dehydrogenase kinases PDK1 and PDK2. Finally, Londergan et al. (DOI: 10.1021/bi5008063) use Raman scattering to characterize the role of a conserved active site thiol in rabbit muscle creatine kinase. The authors find an intrinsic, dynamic asymmetry between the two subunits of the dimeric creatine kinase exists in the apo form of the enzyme. Taken together, these studies utilize a variety of biophysical, computational, molecular, and cellular approaches to provide important new mechanistic insight into kinase function.

Jeffrey L. Benovic
Richard N. Armstrong

AUTHOR INFORMATION

Notes

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