Kinase Templated Abiotic Reaction

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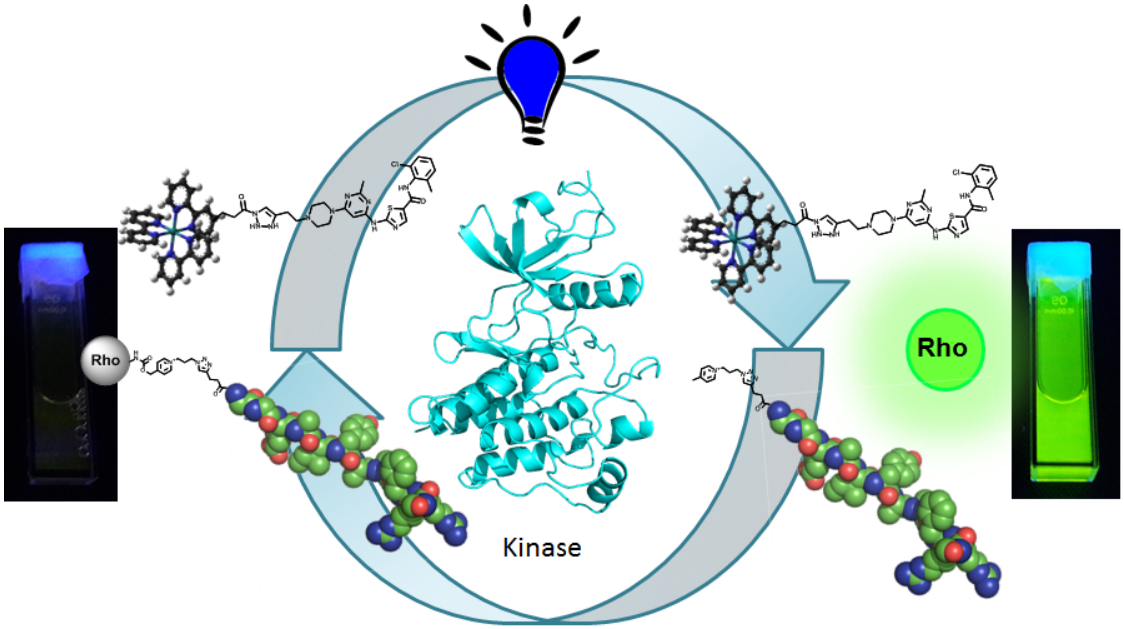
Protein kinases are essential regulators of cellular signalling and have been at the centre stage of drug discovery for the past decade. The successful development of kinase inhibitors demonstrated that kinases were drugable and triggered tremendous research effort in this area. However, inhibitors developed so far often target the conserved ATP binding site of the protein and thus are lacking selectivity[1], and the more selective ones are targeting an inactive form of the protein. These features limit their use as chemical probes to sense kinase activity. Herein we report a strategy[2] based on two reacting probes[3] targeting both nucleotide and substrate binding sites. The reaction[4] used allows to use fluorescence readout to selectively sense Abl of Src kinase activity both in biochemical and fixed whole cell experiments.



[1] O. Hantschel, U. Rix, T. Buerckstuemmer, U. Schmidt, M. Kneidinger, K. L. Bennett, I. Kaupe, W. Ellmeier, P. Valent, G. Superti-Furga, *Blood* **2007**, *110*, 207b-207b.
[2] K. Gorska, I. Keklikoglou, U. Tschulena, N. Winssinger, *Chem Sci* **2011**, *2*, 1969-1975.
[3] K. K. Sadhu, T. Eierhoff, W. Römer, N. Winssinger, *J Am Chem Soc* **2012**, *134*, 20013-20016.
[4] D. Chang, E. Lindberg, N. Winssinger, *J Am Chem Soc* **2017**, *139*, 1444-1447.