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Development of fluorescent probes for cancer cell lines

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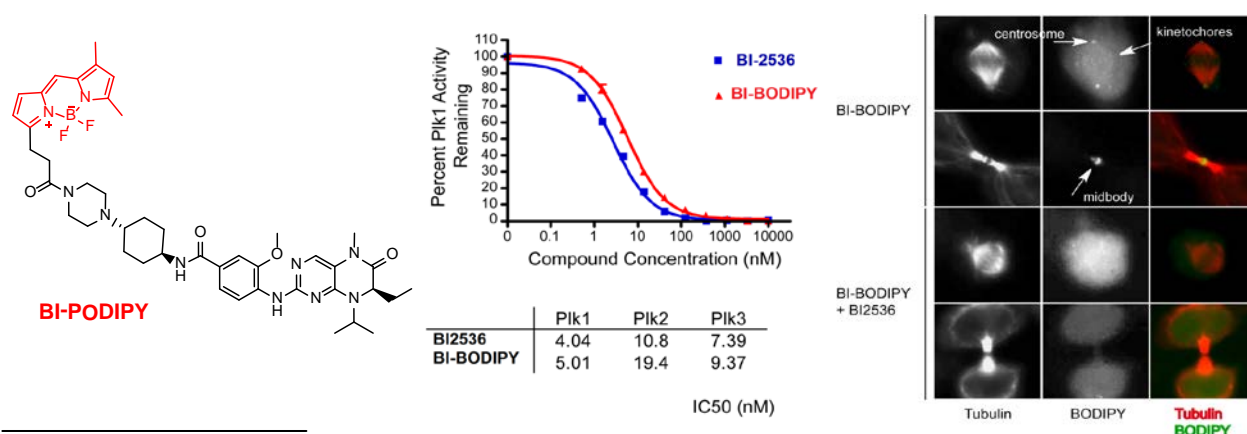
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Abstract: Fluorescence imaging is a powerful tool that permits visualization of specific cell states within a population; however, existing methods for fluorescence labeling cannot be easily applied in many biological systems. Unlike antibodies, small molecule proteins can be cell permeable and therefore useful in live-cell and in vivo imaging experiments; moreover, small molecule probes do not require genetic manipulation of cells.

Protein kinases are in many ways ideal targets for the development of selective fluorescent small molecule probes. This is because protein kinases are involved in most cellular processes and changes in their localization, accessibility, and abundance are associated with changes in cellular state. In addition, drug discovery and chemical biology efforts have in recent decades produced many selective, cell permeable small molecule ligands of specific cellular kinases.

Here we describe our attempts to leverage existing, well-characterized kinase inhibitors to develop fluorescent small molecule probes for use as imaging tools in cancer biology. BODIPY-conjugated kinase inhibitors, such as Mps1-IN-1¹ and BI2536² were synthesized. Their inhibition ability and immunofluorescence staining were tested.³ We demonstrated the utility of BI-BODIPY as a cell permeable probe for monitoring PLK localization. This result serves as the foundation for more sophisticated live-cell and in vivo imaging experiments that we are currently pursuing. This study also provides proof of concept for extension of this strategy to convert other small molecule kinase inhibitors to probes that can analogously be used to monitor localization of their respective kinases.



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