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Et al.

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Polo-like kinase 1 (PLK1) and BRD4 are two different therapeutic targets in cancer drug discovery. Recently it has been reported that PLK1 inhibitor, **BI-2536**, is also a potent inhibitor of BRD4. The simultaneous inhibition of PLK1 and BRD4 by a single drug molecule is interesting because this could lead to the development of effective therapeutic strategy for different types of disease conditions in which PLK1 and BRD4 are implicated. Structural activity relationship studies has been carried out on BI-2536 to generate analogs with enhanced dual inhibitory activity against BRD4 and PLK1 as well as to render the molecule selective to one target over the other. **UMB101** and **160** have been found to exhibit enhanced dual inhibitory activity with selectivity fold of less than 30, **UMB160** being the most potent dual-kinase bromodomain inhibitor (BRD4 IC_{50} = 28 nM, PLK1 IC_{50} = 40 nM). **UMB131** was found to be the most selective PLK1 inhibitor over BRD4.

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