

Title:

MEK1/2-Targeting PROTACs Promote the Collateral Degradation of CRAF in KRAS Mutant Cells

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Withdrawal statement:

Following extensive additional studies, we discovered new findings that suggest that the degradation of CRAF by MS934 is not via collateral degradation through proximity to MEK1/2 but rather via a cell intrinsic mechanism that occurs post MEK1/2 degradation in KRAS mutant cells. We have performed extensive time course experiments exploring MS934-mediated degradation of CRAF, as well as additional MEK1/2 knockdown studies in several cell line models. Data from these studies showed that MEK1/2 proteins are degraded by MS934 several hours before CRAF protein and that genetic depletion of both MEK1 and MEK2 reduces CRAF protein levels equivalent to that observed with MS934. Together, these new findings suggest that CRAF degradation is not due to collateral proximity degradation by MS934 but rather due to a cell intrinsic mechanism post MEK1/2 protein depletion.