Fig. S5.

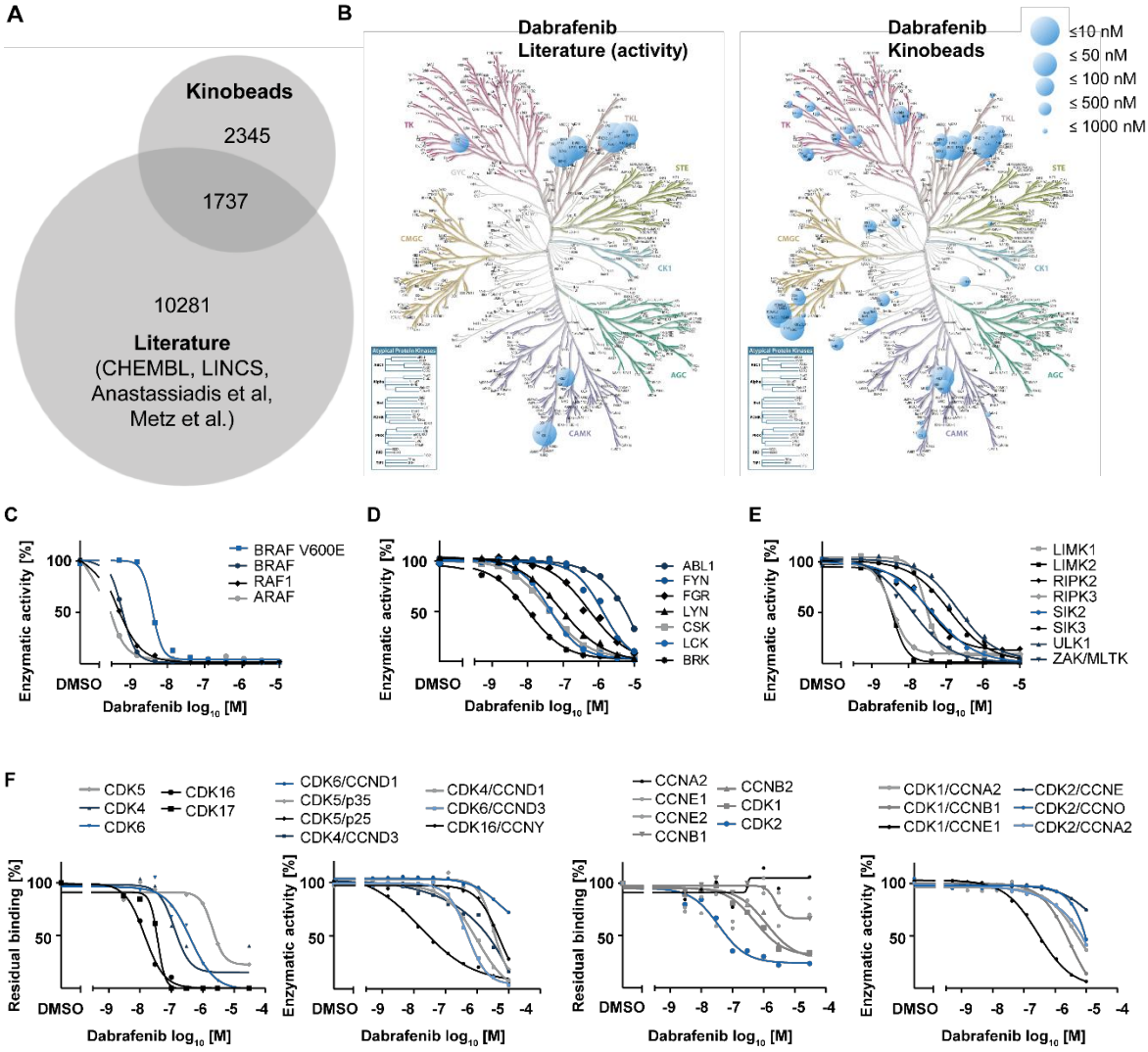

Fig. S5 | Characterization of novel off-targets. (A) Comparison of protein-drug interactions from this study with those described in major publications and online databases (CHEMBL, LINCS, Anastassiadis *et al*., Metz *et al*.) **(B)** Phylogenetic tree representation of all human kinases and Dabrafenib targets (blue) determined from activity (left) and Kinobeads binding data (right; illustration reproduced courtesy of Cell Signaling Technology, Inc; www.cellsignal.com). The size of each circle is proportional to the K_d^{app} of the interaction. **(C-E)** Kinase activity assays of novel Dabrafenib targets validated the binding results obtained with Kinobeads. **(F)** Kinobeads binding and kinase activity assays for Dabrafenib and different CDK/Cyclin combinations. Potent binding competition of CDK2 could not be confirmed in the activity assay).

G

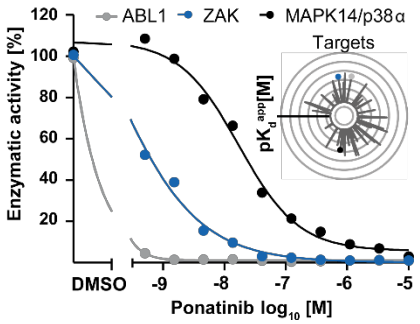

Fig. S5 continued | Characterization of novel off-targets. **(G)** Kinase activity assays for Ponatinib and ABL1, ZAK and MAPK14 confirmed that binding data (inserted radar plot for all kinase targets of Ponatinib) translated into inhibition of kinase activity. The target promiscuity of Ponatinib may be responsible for both desired and undesired side effects.