

Protein abundance of MAPK1 interacting partners ABI1 ARHGEF2 GSK3B CSPG4 19 -18 -17 -16 15 -14 -LRP6 MAP3K3 MAPK1 MAPK3 19 -18 -17 -16 -Protein abundance drug PPARG PRNP MEF2A PTK2 **Trametinib** 17 -16 15 -14 -Untreated -Vemurafenib ^{Trametinib} -Combinations -PXN RPS6KA3 **RPTOR** 19 -18 17 16 -15 -14 -Combinations Vemurafenib Trametinib | Vemurafenib Trametinib Combinations Combinations $U^{ntreated}$ Vemurafenib Trametinib Untreated 4 Drug treatment

RNA expression of MAPK1 interacting partners RPS6KA3 ABI1 MAPK3 **PPARG** PTK2 10.0 7.5 5.0 2.5 0.0 **PXN PRNP** ETS1 MEF2A LRP6 10.0 7.5 5.0 2.5 0.0 DUSP4 MAP3K3 MAPK1 GSK3B **RPTOR** 10.0 RNA expression 7.5 drug 5.0 **□** Untreated **⊭** Vemurafenib 2.5 **Trametinib** 0.0 FOS ARHGEF2 DUSP1 ETS2 HGF 10.0 7.5 5.0 2.5 0.0 CSPG4 DUSP2 DUSP6 IRS1 NR4A2 10.0 7.5 5.0 2.5 0.0 Combinations 1 Combinations Vemurafenib Tametinib Vemurafenib Combinations Vemurafenib Combinations Trametinib Tametinib Vemurafenib + Combinations -Untreated 1 $U^{ntreated}$ Tametinib | Untreated 1 Untreated + Untreated |

Protein abundance of EGFR interacting partners ABL2 EGFR FGFR1 19 -18 17 16 15 -GPNMB ICAM1 FYN 19 · Protein abundance drug Untreated Vemurafenib Trametinib 15 -PRKD1 PARP1 **PTPRJ** 19 18 -17 -16 15 -Combinations Combinations Combinations Vemurafenib -Untreated | Vemurafenib Trametinib | Vemurafenib Trametinib Untreated 4 Trametinie Untreated 1 Drug treatment

RNA expression of EGFR interacting partners ABL2 FYN EGFR **PTPRJ** 10 -5 0 NTRK2 FGFR1 PARP1 SOX2 10 -0 -RNA expression drug **□** Untreated ANG TEK ICAM1 EGF Vemurafenib **Trametinib** 5 0 -Combinations -Vemurafenib + Trametinib Untreated -Trametinib -Combinations -**GPNMB** PRKD1 10 -5 -0 -Trametinib Combinations -Combinations -Vemurafenib Trametinib Drug treatment



