PYK2/FAK inhibitors reverse hypoxia-induced drug resistance in multiple myeloma

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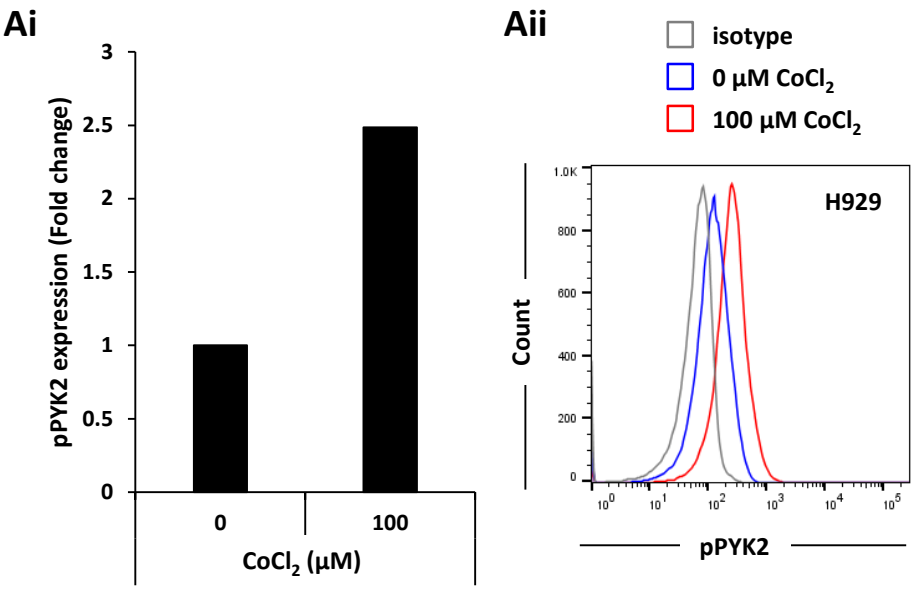
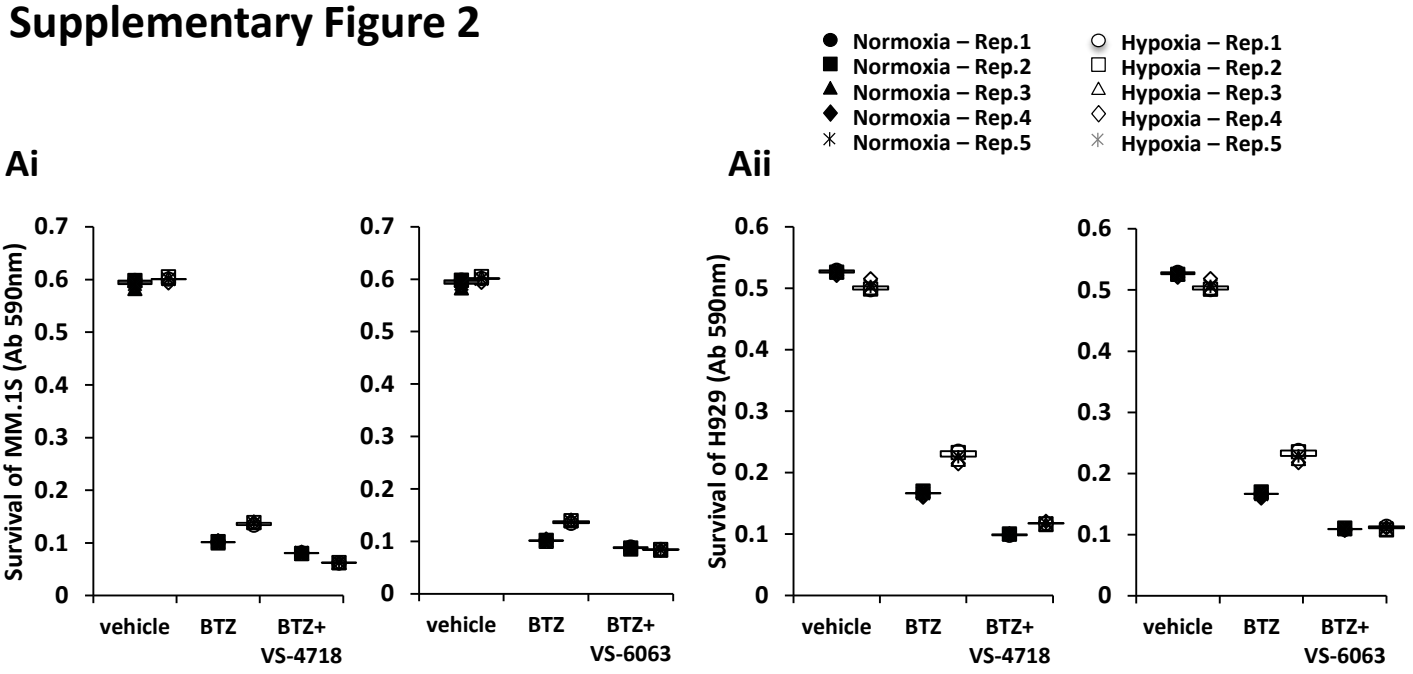
doi:10.3324/haematol.2018.194688

Supplementary Figure 1



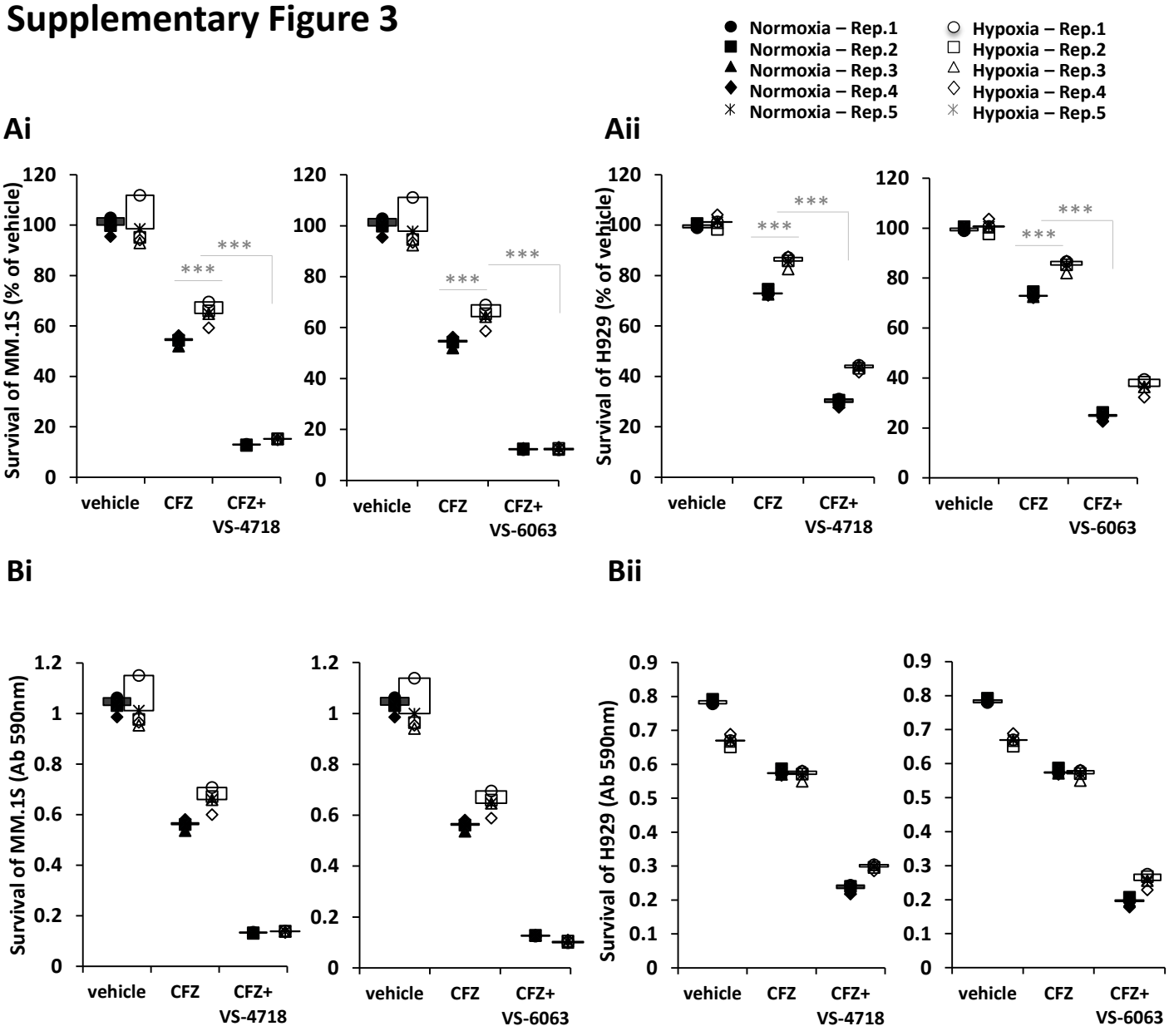
Supplementary Figure 1 Hypoxia induces pPYK2 expression in H929 cells. Expression of intracellular pPYK2 in H929 cell line untreated or treated with 100 µM $CoCl_2$ in normoxia for 24 hours demonstrated as a fold change of expression (relative to untreated) **(Ai)** and histogram **(Aii)** using flow cytometry.

Supplementary Figure 2



Supplementary Figure 2 VS-4718 and VS-6063 combined with bortezomib (BTZ) overcome hypoxia-induced drug resistance in MM cells *in vitro*. Absorbance readout (Ab 590nm) of MTT assay performed on MM.1S **(Ai)** and H929 **(Aii)** treated with VS-4718 (2.5 μM) or VS-6063 (2.5 μM) and in combination with bortezomib (5nM). Results are shown as average ± standard deviation (SD) performed in penta-replicates and repeated minimum in three separate experiments.

Supplementary Figure 3



Supplementary Figure 3 VS-4718 and VS-6063 combined with carfilzomib (CFZ) overcome hypoxia-induced drug resistance in MM cells *in vitro*. Survival of MM.1S cells treated with VS-4718 (2.5 µM) or VS-6063 (2.5 µM) and in combination with carfilzomib (5 nM) **(Ai)**; and H929 cells treated with VS-4718 (2.5 µM) or VS-6063 (2.5 µM) and in combination with carfilzomib (2 nM) **(Aii)**, cultured for 24 hours in normoxic and hypoxic conditions based on a survival/cytotoxic MTT assay. Absorbance readout of MTT assay performed on MM.1S **(Bi)** and H929 **(Bii)** treated with either VS-4718 and VS-6063 and combined with carfilzomib. Results are shown as average ± standard deviation (SD) performed in penta-replicates and repeated minimum in three separate experiments; the statistical significance was assessed by student t-test (*** $p<0.001$).