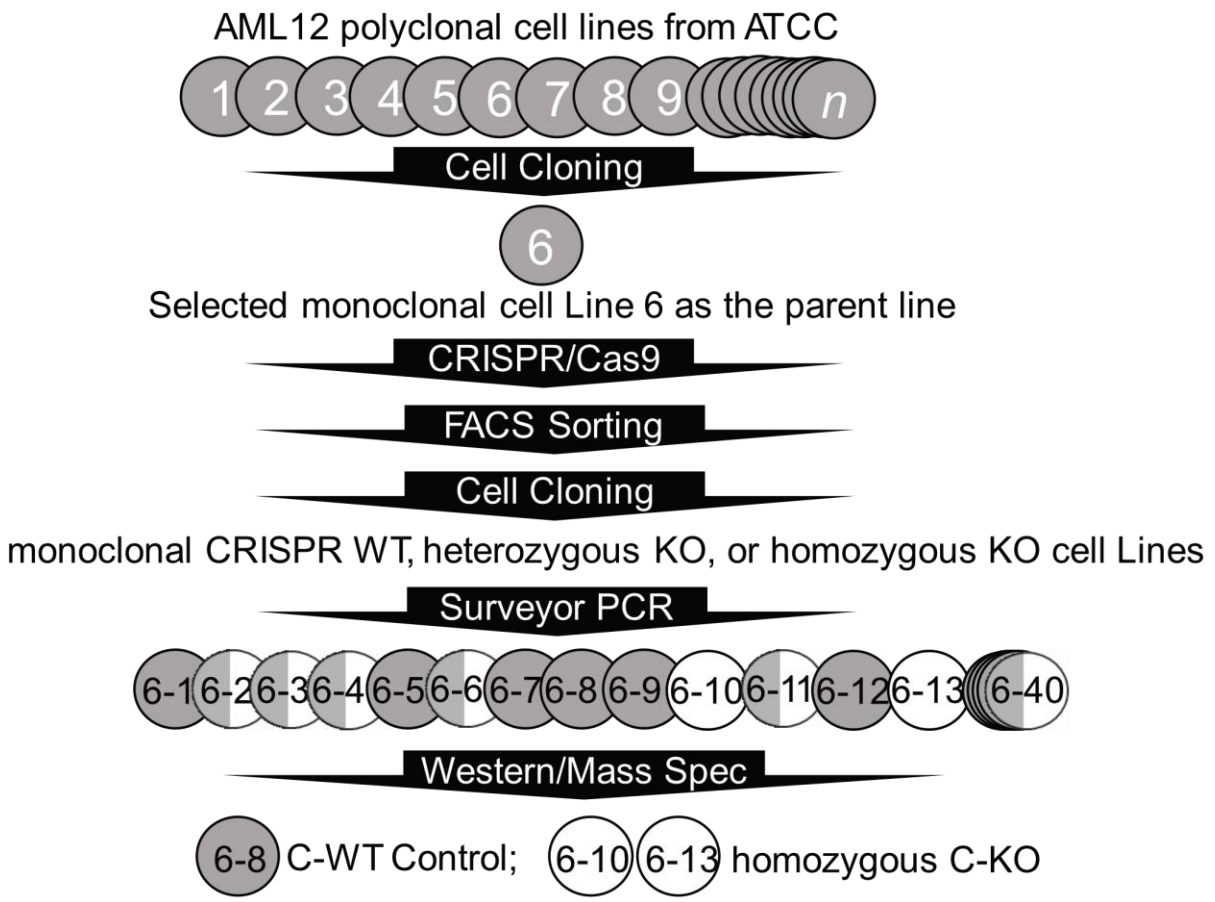

Figure S1. Cell cloning strategy for CRISPR/Cas9 deletion of VWA8. Monoclonal parent cell line 6 was created by limiting dilution from stock polyclonal AML12 cells and was used to create CRISPR knockout (KO) and CRISPR wildtype (WT) control cells. CRISPR wildtype cells are cells that underwent the CRISPR/Cas9 process without successful deletion of VWA8. Subsequent analysis showed these cells to be equivalent to the parent cell line. Confirmation of deletion of VWA8 gene (Surveyor PCR) and protein (Western blot, mass spectrometry yielded CRISPR wildtype cell line 6-8 and CRISPR knockout cell lines 6-10 and 6-13.

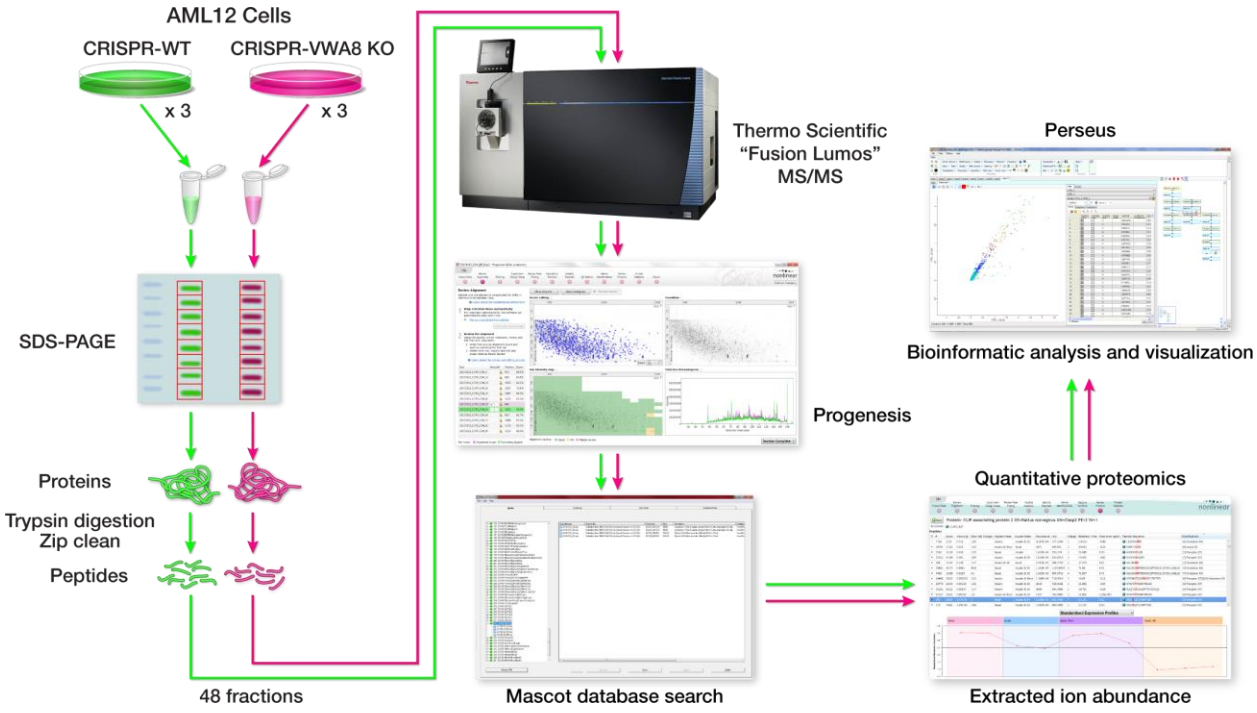

Figure S2. Proteomics workflow.

Table S9. Comparison of Seahorse respiration results in differentiated, permeabilized wildtype and VWA8-null AML12 hepatocytes.

	Pyruvate, malate, glutamate			Palmitoyl-carnitine, malate		
	WT	KO	KO/WT (fold)	WT	KO	KO/WT (fold)
Basal	62 ± 12	147 ± 14**	2.37	94 ± 8	266 ± 8***	2.83
Maximum ADP stimulated respiration	397 ± 40	1478 ± 9***	3.72	345 ± 13	891 ± 20***	2.58
Proton leak	55 ± 8	117 ± 18*	2.14	58 ± 5	133 ± 6***	2.30
Maximum (FCCP)	681 ± 126	1609 ± 32***	2.36	765 ± 68	1073 ± 45*	1.40
Non-mitochondrial	71 ± 8	174 ± 10***	2.45	77 ± 5	196 ± 4***	2.55

Rates of respiration in wildtype (WT) and VWA8 null (KO) differentiated AML12 cells Data are given as Means ± SEM in units of pmol O_2 consumption per minute. N = 5 experiments, *P<0.01, **P<0.001, ***P<0.0001 vs. wildtype. Statistical analysis was done using t-tests. Pyruvate (5 mM), malate (1.0 mM), and glutamine (10 mM) were used for carbohydrate fuel; palmitoyl–CoA (40 µM), carnitine (0.5 mM) and malate (1.0 mM) were used for lipid fuel. Concentrations of ADP, oligomycin, FCCP, ADP and rotenone/antimycin A are given in the methods.