Supplemental Material

Fig. S1

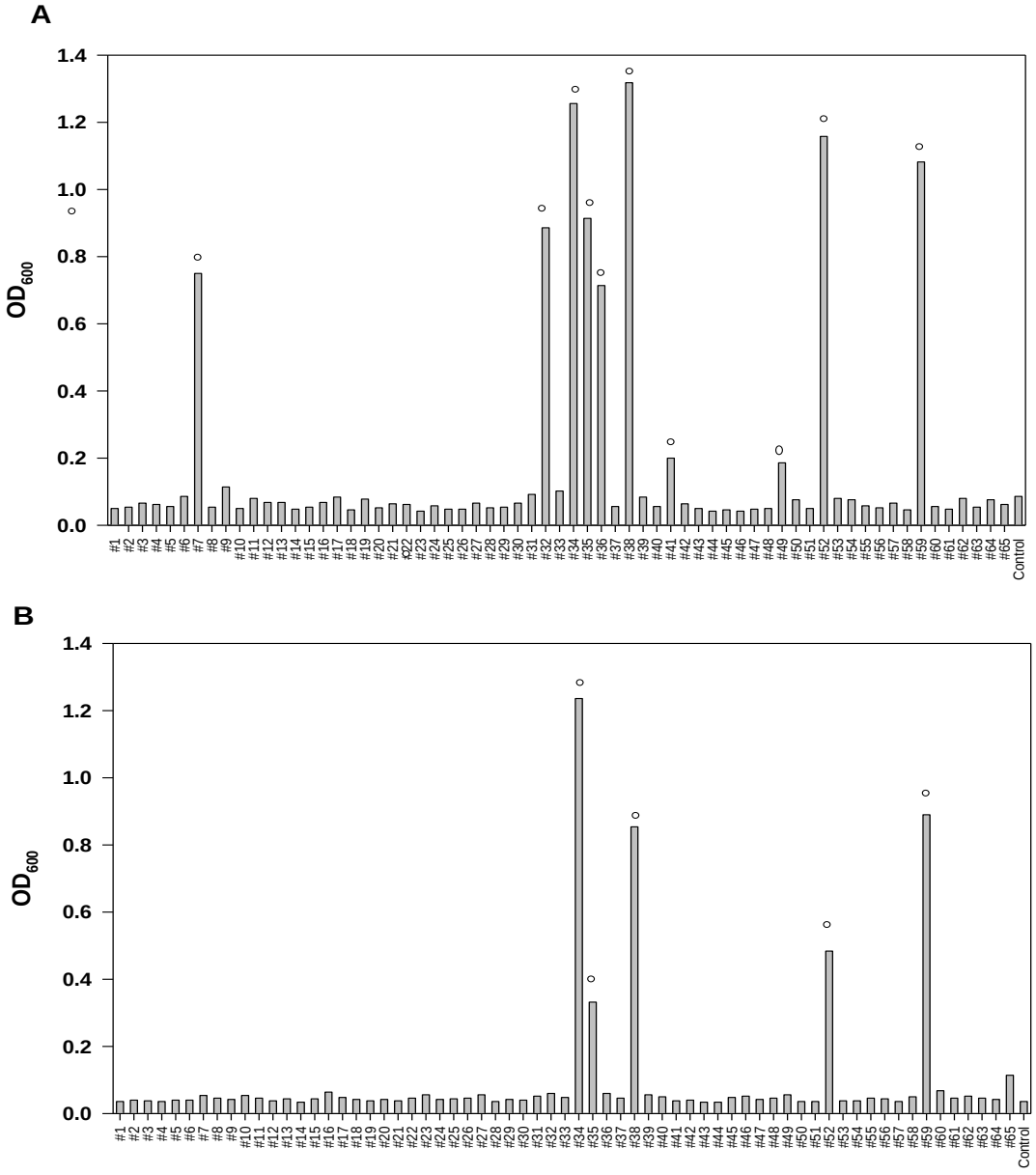

Figure S1. Cell growth performances of 65 yeast genomic library transformants in SC media containing glucose (20 g/L)+acetic acid (2.5 g/L) (A), or xylose (20 g/L)+acetic acid(2.5 g/L) (B). Cell growths were measured at 60 hr (A) or 106 hr (B). The hollow circles present the selected fast-growing transformants.

Fig. S2

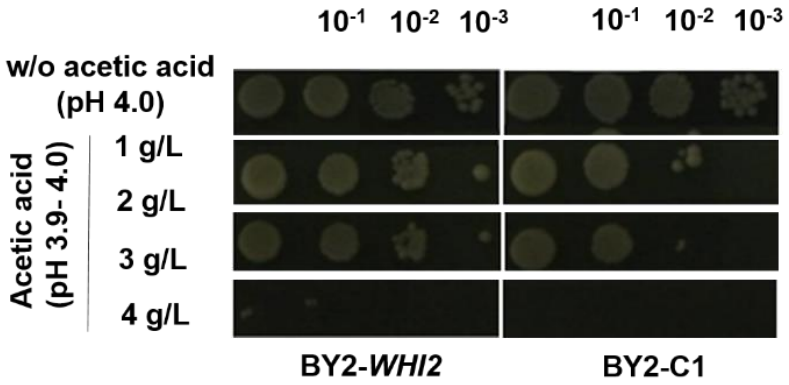

Figure S2. Increased cell growth conferred by overexpressing *WHI2* in the strain BY4742. Cells were grown on minimal medium agar plates containing glucose (20 g/L), amended with various concentrations of acetic acid or without acetic acid. Cells of the strain BY2-*WHI2* or the control strain BY2-C1 were spotted with serial dilution by a factor of 10.

Fig. S3

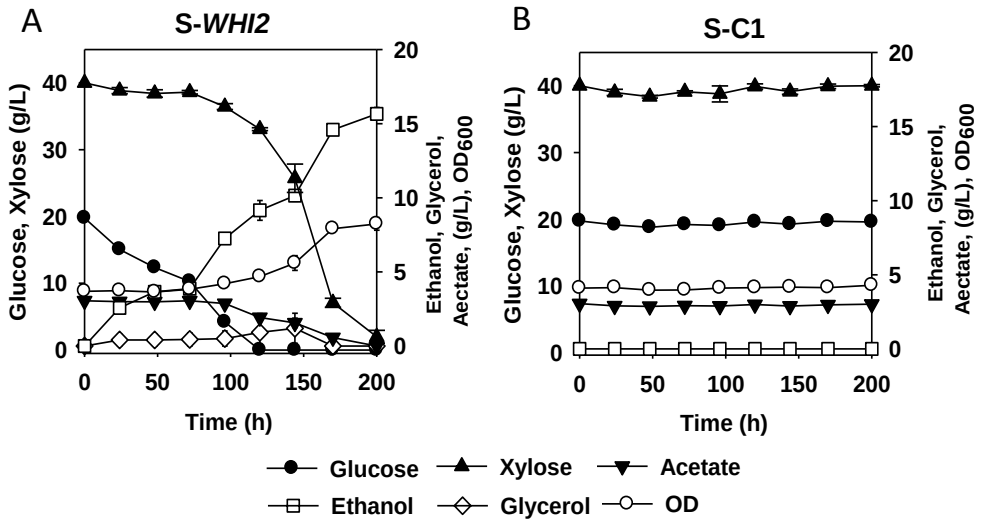

Figure S3. Improved fermentation by the strain S-*WHI2* (A) compared to the control strain S-C1 (B) in corn stover hydrolysate with 50% v/v YP medium under oxygen limited condition. Results are the means of duplicate experiments; error bars indicating standard deviations are not visible when smaller than the symbol size.

Fig. S4

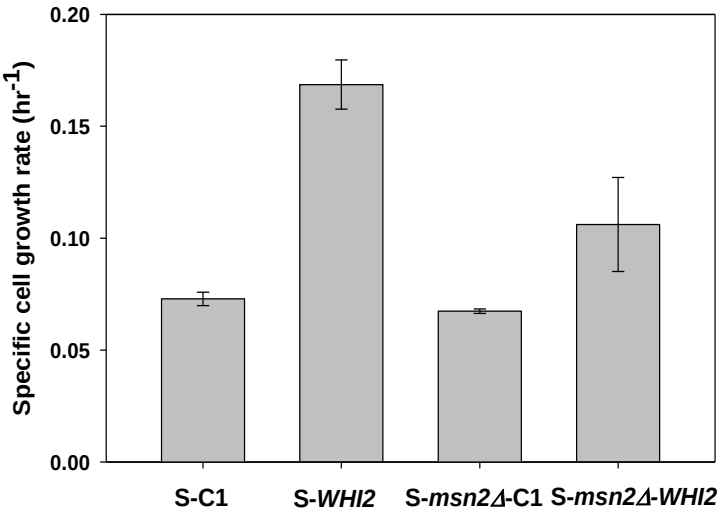

Figure S4. Specific cell growth rates of the strains S-C1, S-*WHI2*, S-*msn2Δ*-C1 and S-*msn2Δ*-*WHI2* in SC media containing glucose (20 g/L) with 2 g/L acetic acid. Results are the means of triplicate experiments; error bars indicate standard deviations.

Fig. S5

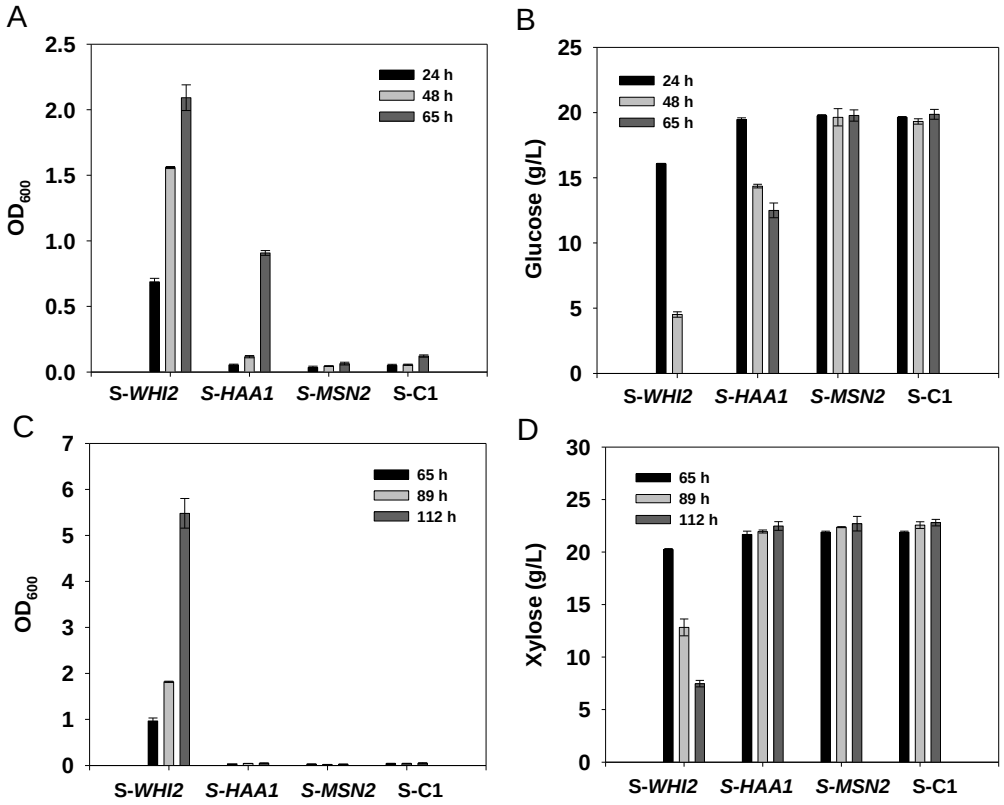

Figure S5. Acetic acid resistance of the engineered strains overexpressing the selected gene targets in SC media containing glucose (A and B) or xylose (C and D) with 2.5 g/L acetic acid. Cell growth (A and C) and sugar consumption (B and D) were measured. Results are the means of triplicate experiments; error bars indicating standard deviations are not visible when smaller than the symbol size.

Table S1. Primers for PCR amplification and sequencing

Target	Primer sequence
WHI2	Forward GCCGGATCCAAAAATGGACGATATAATCACGCAAG
	Reverse GCCGTCGACTCACTGCACCCCAATAACGC
HAA1	Forward GCCACTAGTATGGTCTTGATAAATGGCATAAAG
	Reverse GCCGGATCCTCATAACGAAGACATGAAATTATC
MSN2	Forward GCCACTAGTATGACGGTCGACCATGATTTC
	Reverse GCCGGATCCTTAAATGTCTCCATGTTTTTTATG
PSR1	Forward GCCGGATCCAAAAATGGGTTTCATATCGTCAATACTG
	Reverse GCCGTCGACTTATATTGTTACATCCAAAATTTTGC
msn2-F	CCTTGGAGATAACAGAAACTAGTC
msn2-R	Reverse CGTGTATCTAAGTTGTTACAGGC
T3 promoter	AATTAACCCTCACTAAAGGG
T7 promoter	TAATACGACTCACTATAGGG
WHI2 (q-PCR)	Forward TCTTCGGCTCTTGGAAAGAT
	Reverse AATCGGACGGGTACAATGAT
UBC6 (q-PCR)	Forward TACAAACCACCGGCTATCAG
	Reverse CCAGCCAGGATTCCAAGTAT

Table S2. Summary of fermentation performances of the strains S-*WHI2* and S-C1 under different conditions.

Sugar	Condition	Strains	μ*	$Y_{ethanol}$	r_{sugar}*	$P_{ethanol}$*	pH_0	pH_t
20 g/l Glucose	**No acetic acid under oxygen limited condition**	S-*WHI2*	0.087±0.002	0.344±0.007	1.625±0.003	0.537±0.012	3.98±0.000	3.51±0.000
		S-C1	0.089±0.002	0.356±0.002	1.739±0.021	0.619±0.004	3.98±0.000	3.56±0.007
	2.5 g/L acetic acid under oxygen limited condition	S-*WHI2*	0.030±0.001	0.456±0.002	1.846±0.019	0.842±0.011	4.01±0.000	3.32±0.007
		S-C1	n.d.	0.373±0.000	0.355±0.000	0.130±0.003	4.01±0.000	3.75±0.000
	2.5 g/L acetic acid under anaerobic condition	S-*WHI2*	0.025±0.002	0.502±0.010	1.991±0.024	0.999±0.008	4.01±0.000	3.23±0.001
		S-C1	n.d.	0.451±0.008	0.399±0.003	0.180±0.008	4.01±0.000	3.81±0.000
20 g/l Xylose	**No acetic acid under oxygen limited condition**	S-*WHI2*	0.046±0.003	0.227±0.016	0.464±0.025	0.092±0.012	4.00±0.000	3.41±0.000
		S-C1	0.049±0.001	0.232±0.015	0.428±0.016	0.099±0.010	4.00±0.000	3.46±0.005
	2.5 g/L acetic acid under oxygen limited condition	S-*WHI2*	0.015±0.000	0.278±0.017	0.245±0.004	0.068±0.005	4.01±0.000	3.28±0.000
		S-C1	0.003±0.001	n.d.	n.d.	n.d.	4.01±0.000	3.81±0.000
	1.5 g/L acetic acid under anaerobic condition	S-*WHI2*	0.001±0.000	0.328±0.013	0.227±0.031	0.074±0.007	3.99±0.000	3.40±0.001
		S-C1	0.001±0.000	0.339±0.003	0.195±0.000	0.066±0.001	3.99±0.000	3.54±0.002

Note:

μ*: specific growth rate (hr^{-1});

$Y_{ethanol}$: ethanol yield (g ethanol/g sugar);

r_{sugar}*: specific sugar consumption rate (g sugar/g dry cell wt/hr);

$P_{ethanol}$*: specific ethanol productivity (g ethanol/g dry cell wt/hr);

pH_0: initial pH;

pH_t: pH at the end of fermentation.