Electronic Supplementary Material (ESI) for Metallomics.


**Table S1** Comparison of major metabolites quantified through GC-MS and LC-QqQ-MS between control and zinc addition based on various cell growth stages[§] ([*] $p<0.05$).

| Metabolites (nmol/g DCW) | | Stage I (0.1 g/L biomass) | | | Stage II (1.5 g/L biomass) | | | Stage III (3.0 g/L biomass) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | CK | Zn | Ratio (Zn/CK) | CK | Zn | Ratio (Zn/CK) | CK | Zn | Ratio (Zn/CK) |
| Glycolysis | G6P | 7.44±2 | 5.19±2 | 0.70 | 0.69±0.1 | 1.78±0.1 | **2.58**[*] | 1.17±0.5 | 1.27±0.6 | 1.09 |
| | F6P | 0.87±0.2 | 0.59±0.1 | 0.68 | 0.26±0.1 | 0.64±0.0 | **2.46**[*] | 0.86±0.3 | 0.41±0.1 | 0.48 |
| | FBP | 1.04±0.4 | 0.71±0.1 | 0.68 | 0.11±0.1 | 0.18±0.01 | 1.64 | 0.49±0.4 | 0.06±0.04 | 0.12 |
| | 2PGA | 0.59±0.4 | 0.30±0.3 | 0.51 | 0.073±0.1 | 0.2±0.3 | 2.74 | 0.11±0.1 | 0.062±0.1 | 0.56 |
| | PEP | 0.65±0.4 | 0.22±0.1 | 0.34 | 0.17±0.1 | 0.25±0.1 | 1.47 | 0.23±0.1 | 0.16±0.04 | 0.70 |
| PP-pathway | Ru5P | 0.44±0.2 | 0.081±0.03 | 0.18 | 0.11±0.1 | 0.20±0.1 | 1.82 | 0.29±0.2 | 0.26±0.1 | 0.90 |
| | R5P | 0.53±0.3 | 0.18±0.1 | 0.34 | 0.06±0.03 | 0.08±0.01 | 1.33 | 0.08±0.03 | 0.05±0.01 | 0.63 |

**Table S1** continued

| Metabolites (nmol $g^{-1}$ DCW) | | Stage I (0.1 g $L^{-1}$ biomass) | | | Stage II (1.5 g $L^{-1}$ biomass) | | | Stage III (3.0 g $L^{-1}$ biomass) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | CK | Zn | Ratio (Zn/CK) | CK | Zn | Ratio (Zn/CK) | CK | Zn | Ratio (Zn/CK) |
| PP-pathway | Xu5P | 0.73±0.1 | 0.27±0.03 | **0.37*** | 0.15±0.03 | 0.27±0.01 | **1.80*** | 0.40±0.05 | 0.34±0.01 | 0.85 |
| | S7P | 0.50±0.2 | 0.23±0.1 | 0.46 | 0.073±0.05 | 0.14±0.1 | 1.92 | 0.16±0.1 | 0.35±0.1 | 2.19 |
| | E4P | 0.64±0.3 | 0.16±0.1 | 0.25 | 0.060±0.1 | 0.082±0.01 | 1.37 | 0.03±0.01 | 0.03±0.01 | 1.00 |
| Amino acids | Val | 264.0±29 | 392.65±0.0 | **1.49*** | 14.41±3 | 15.13±0.4 | 1.05 | 4.31±0.3 | 8.25±0.2 | **1.91*** |
| | Gly | 654.87±95 | 806.18±14 | 1.23 | 55.96±7 | 42.01±1.5 | 0.75 | 20.02±3 | 33.78±3 | **1.69*** |
| | Ser | 362.22±16 | 446.23±7 | **1.23*** | 22.17±2 | 22.73±0.6 | 1.03 | 11.69±0.4 | 21.00±1.1 | **1.80*** |
| | Proline | 310.04±14 | 270.88±0.0 | 0.87 | 23.04±2.6 | 23.69±0.5 | 1.03 | 12.56±0.9 | 13.71±1.1 | 1.09 |
| Others | Trehalose | 202.43±20 | 320.12±14 | **1.58*** | 33.43±2.7 | 26.93±1.1 | 0.81 | 292.88±65 | 211.98±46 | 0.72 |

**Table S1** continued

| Metabolites | | Stage I (0.1 g $L^{-1}$ biomass) | | | Stage II (1.5 g $L^{-1}$ biomass) | | | Stage III (3.0 g $L^{-1}$ biomass) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| (nmol $g^{-1}$ DCW) | | CK | Zn | Ratio (Zn/CK) | CK | Zn | Ratio (Zn/CK) | CK | Zn | Ratio (Zn/CK) |
| Others | Mannose | 370.70±156 | 308.76±7 | 0.83 | 41.50±6.4 | 32.18±9.7 | 0.78 | 12.88±2.1 | 9.52±0.98 | 0.74 |
| | Fructose | 3913.74±32 | 5444.41±21 | **1.39*** | 287.94±7.5 | 220.17±15 | **0.76*** | 82.54±18 | 23.13±5.9 | **0.28*** |
| | GSSG | 490.71±174 | 303.31±103 | 0.62 | 98.14±50 | 160.90±54 | 1.64 | 163.94±10 | 242.80±7.6 | **1.48*** |
| | GABA | 238.35±29 | 337.36±43 | 1.42 | ND | 31.44±5.2 | | ND | 16.85±0.3 | |
| | $NAD^+$ | 26.13±20 | 12.05±9.4 | 0.46 | 4.16±2.9 | 6.39±4.7 | 1.54 | 3.56±2.6 | 3.26±2.2 | 0.92 |
| | NADH | 0.38±0.1 | 0.29±0.1 | 0.76 | 0.06±0.03 | 0.16±0.1 | 2.67 | 0.33±0.1 | 0.25±0.1 | 0.76 |
| | $NADP^+$ | 0.61±0.1 | 0.12±0.03 | **0.20*** | 0.17±0.02 | 0.14±0.1 | 0.82 | 0.069±0.01 | 0.015±0.001 | **0.21*** |
| | NADPH | 0.11±0.1 | 0.01±0.01 | 0.09 | 0.01±0.002 | 0.01±0.002 | 0.94 | 0.01±0.001 | 0.001±0.001 | 0.26 |

[§]ND, not detectable.

## Supplementary figures

**Fig. S1.** Overview of the number of unique metabolites and common metabolites at different growth stages in control and zinc-supplemented cells.

Numbers in grey and orange background means numbers of the unique metabolites detected in the control and zinc-supplemented cells at different cell growth stages, respectively, whereas numbers in green background indicate numbers of common metabolites with or without zinc addition.

**Fig. S2.** Effects of serine (A) and valine (B) addition on the glucose consumption of *S. cerevisiae* SPSC01 in presence of 7.5 g $L^{-1}$ acetic acid.

The concentrations of serine and valine used in this study were (g $L^{-1}$): 0, 0.2, 0.5 and 1.0, respectively. Acetic acid was added at the final concentration of 7.5 g $L^{-1}$ in the culture medium after autoclaving and cooling the medium to room temperature. Yeast strain of SPSC01 was activated in seed medium by overnight cultivation for two times, which was then deflocculated by 0.2 M sodium citrate, and the initial inoculum was adjusted to $OD_{620nm}$ of 2.0. Five milliliter of the seed culture was inoculated to 250 ml flasks containing 100 ml fermentation medium and the culture was incubated at 150 rpm, 30 ℃ for 66 h. Samples were collected at a 12 h interval, and residual glucose concentrations were determined.

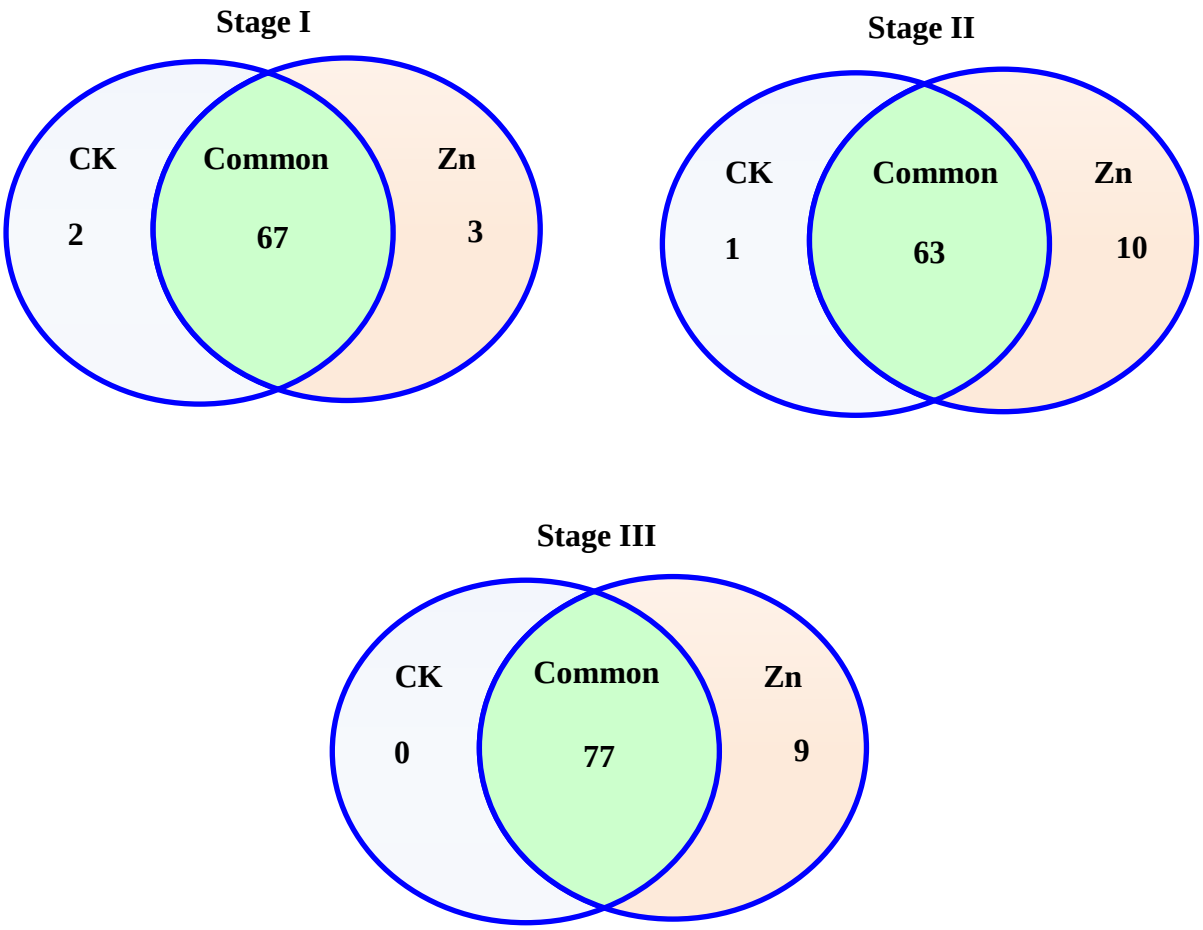
Stage I
CK
2
Common
67
Zn
3
Stage II
CK
1
Common
63
Zn
10
Stage III
CK
0
Common
77
Zn
9

**Fig. S1.**

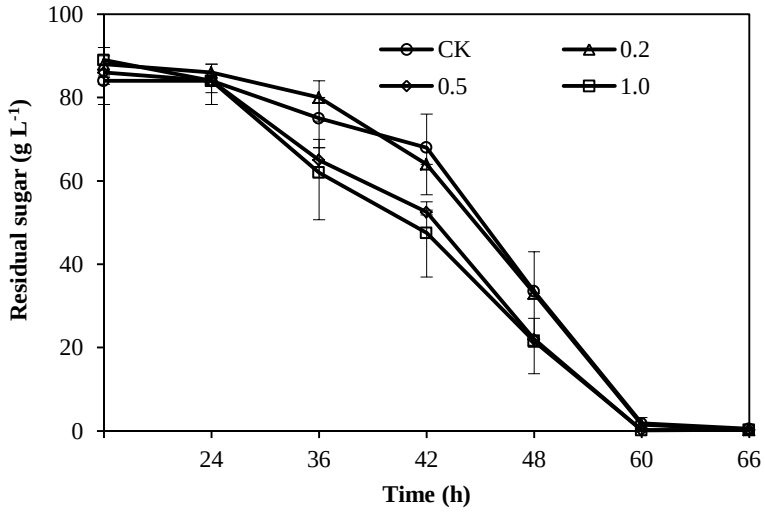
100
80
60
40
20
0
Residual sugar (g L-1)
CK
0.2
0.5
1.0
24
36
42
48
60
66
Time (h)

**Fig. S2A**

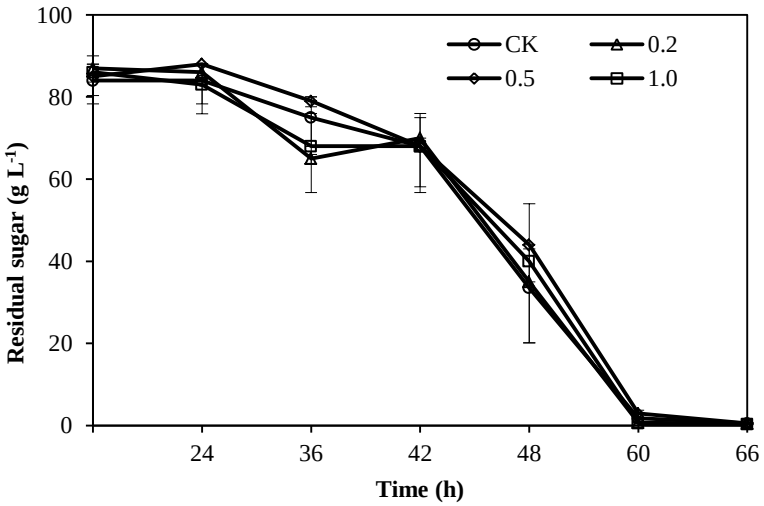
100
80
60
40
20
0
Residual sugar (g L-1)
24
36
42
48
60
66
Time (h)
CK
0.2
0.5
1.0

**Fig. S2B**