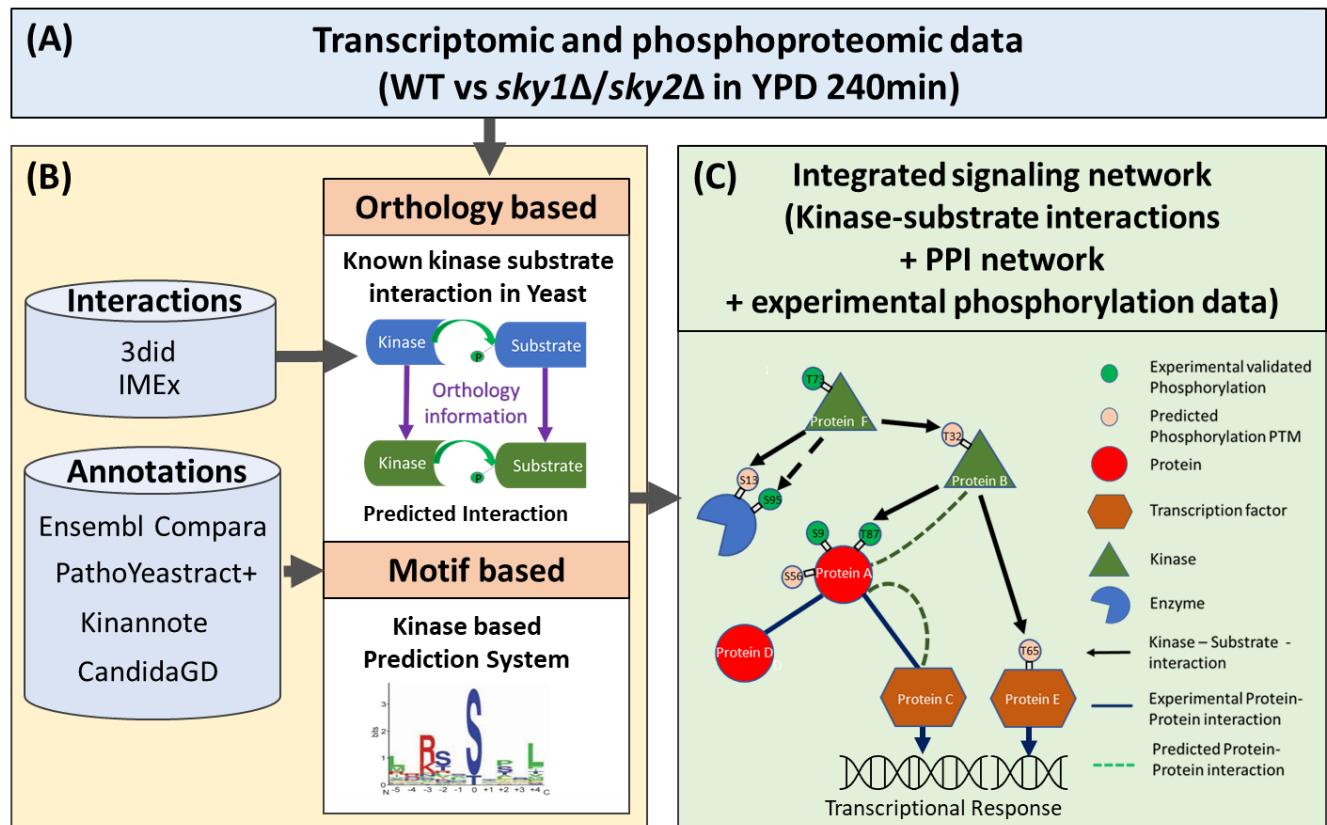


Supplementary Material

1 Supplementary Figures and Tables

1.1 Supplementary Figures



Supplementary Figure 1: Concept of the integrated signaling module construction. (A) Quantitative differential gene expression and phosphorylation analysis of *sky1Δ* and *sky2Δ* versus WT in YPD after 4 hours. (B) For differentially expressed and phosphorylated genes and proteins, site-specific kinase-substrate interactions predictions were performed by interolog transfer as well as sequence motif-based analysis and complemented by the collection of experimentally known protein-protein interactions from literature. (C) Construction of a *sky1Δ* and *sky2Δ* integrated signaling modules based on predicted und experimentally validated interactions and omics data

2 Supplementary Tables

Supplementary Table 1: *C. albicans* strains used in this study

Strain	Genotype	Parental strain	Reference
SC5314	wild type	–	(Gillum et al., 1984)
<i>sky1Δ A</i>	<i>sky1Δ::FRT/sky1Δ::FRT</i>	SC5314	(Ramirez-Zavala et al., 2022)
<i>sky2Δ A</i>	<i>sky2Δ::FRT/sky2Δ::FRT</i>	SC5314	(Ramirez-Zavala et al., 2017)
<i>sky1Δ + SKY1 A</i>	<i>sky1Δ::FRT/SKY1-FRT</i>	<i>sky1Δ A</i>	(Brandt et al., 2022)
<i>sky2Δ + SKY2 A</i>	<i>sky2Δ::FRT/SKY2-FRT</i>	<i>sky2Δ A</i>	(Brandt et al., 2022)

Supplementary Table 2: Detailed information for direct protein-protein interactions (Figure 4,5) based on IMEx (Orchard et al., 2012)

Interactor A	Interactor B	Experimental system	References	Species
Ace2	Cst20	Two-hybrid, Affinity Capture-Western	(van Wijlick et al., 2016)	<i>C. albicans</i>
Ace2	orf19.3626	Two-hybrid	(van Wijlick et al., 2016)	<i>C. albicans</i>
Ace2	She3	Two-hybrid	(van Wijlick et al., 2016)	<i>C. albicans</i>
Efg1	Czf1	Two-hybrid	(Giusani et al., 2002; Noffz et al., 2008; Petrovska and Kumamoto, 2012; Frazer et al., 2020)	<i>C. albicans</i>
Efg1	Flo8	Two-hybrid, Affinity Capture-Western	(Cao et al., 2006; Noffz et al., 2008)	<i>C. albicans</i>
Efg1	Sfl2	Affinity Capture-Western	(Znaidi et al., 2013)	<i>C. albicans</i>
Efg1	Wor1	Affinity Capture-MS	(Alkafeef et al., 2018)	<i>C. albicans</i>
Flo8	Efg1	Two-hybrid, Affinity Capture-Western	(Cao et al., 2006; Noffz et al., 2008)	<i>C. albicans</i>
Flo8	Mfg1	Affinity Capture-MS	(Ryan et al., 2012)	<i>C. albicans</i>

Supplementary Table 3: Detailed information for direct regulatory interactions (Figure 4) based on PathoYeasttract+ (Monteiro et al., 2020)

Transcription factor	Target gene	Regulation type	Experimental system	References	Species
Ace2	Cup9	Direct	Chip-on-chip	(Desai et al., 2015)	<i>C. albicans</i>
Ace2	Efg1	Direct	Chip-on-chip	(Desai et al., 2015)	<i>C. albicans</i>
Ace2	Flo8	Direct	Chip-on-chip	(Desai et al., 2015)	<i>C. albicans</i>
Ace2	Wor1	Direct	Chip-on-chip	(Desai et al., 2015)	<i>C. albicans</i>
Efg1	Ace2	Direct	Chip-on-chip	(Saputo et al., 2014)	<i>C. albicans</i>
Efg1	Cup9	Direct	Chip-on-chip	(Lassak et al., 2011; Nobile et al., 2012; Desai et al., 2015)	<i>C. albicans</i>
Efg1	Flo8	Direct	Chip-on-chip	(Nobile et al., 2012)	<i>C. albicans</i>
Efg1	Sfl2	Direct	Chip-on-chip	(Nobile et al., 2012)	<i>C. albicans</i>
Efg1	Wor1	Direct	Chip-on-chip	(Lassak et al., 2011; Nobile et al., 2012; Hernday et al., 2013)	<i>C. albicans</i>
Flo8	Cup9	Direct	Chip-on-chip	(Polvi et al., 2019)	<i>C. albicans</i>
Flo8	Efg1	Direct	ChIP	(Fox et al., 2015)	<i>C. albicans</i>
Flo8	Mac1	Direct	Chip-on-chip	(Polvi et al., 2019)	<i>C. albicans</i>
Flo8	Pho4	Direct	Chip-on-chip	(Polvi et al., 2019)	<i>C. albicans</i>
Sfl1	Flo8	Direct	ChIP	(Znaidi et al., 2013)	<i>C. albicans</i>
Wor1	Cup9	Direct	ChIP	(Zordan et al., 2007; Hernday et al., 2013)	<i>C. albicans</i>
Wor1	Efg1	Direct	RT-PCR - wt vs mutant promoter sequence, ChIP, Tandem affinity HBH purification coupled with mass spectroscopy	(Zordan et al., 2006; Zordan et al., 2007; Hernday et al., 2013; Alkafeef et al., 2018)	<i>C. albicans</i>

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