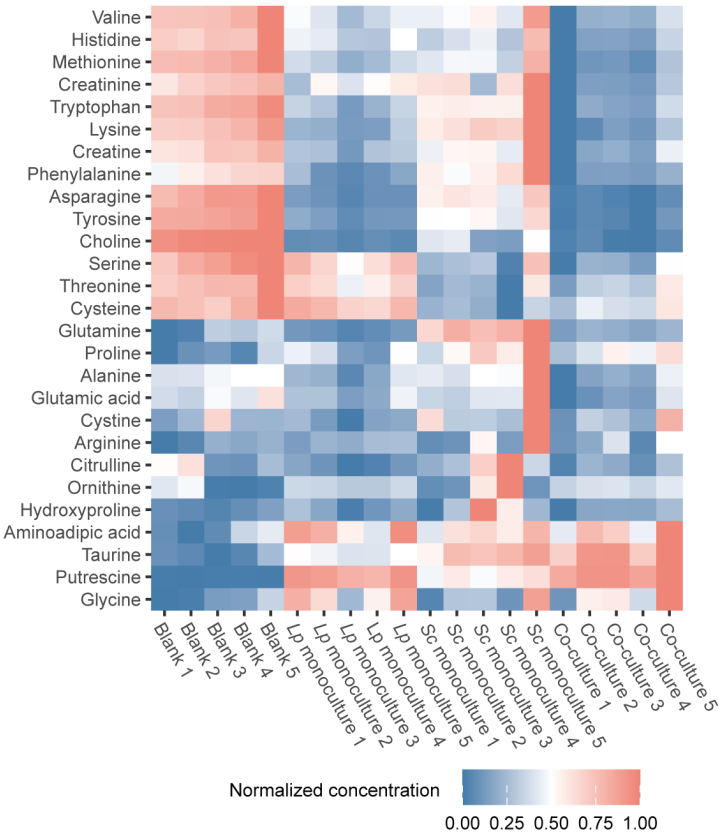

Supplementary Fig. 1: Metabolomic analysis of synthetic sourdough starter.
Targeted metabolomics of amino acids in synthetic starter from blank medium, *L. plantarum* mono-culture, *S. cerevisiae* mono-culture, and co-culture (mean ± sd, n = 5 starters).

a

Minimized GPCR signalling pathway

	Spacer 1: reporter			Spacer 2: Gα (Gpa1 chimera)			Spacer 3: Receptor			Spacer 4: TF		
Design 1	P_{FUS1}	sfGFP	T_{TDH1}	P_{PGK1}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (human)	T_{SSA1}	P_{RAD27}	STE12	T_{ENO1}
Design 2	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{PGK1}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (human)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}
Design 3	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{ALD6}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (human)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}
Design 4	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{ALD6}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (mouse)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}
Design 5	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{ALD6}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (olive baboon)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}
Design 6	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{ALD6}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (green monkey)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}
Design 7	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{ALD6}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (cat)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}
Design 8	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{ALD6}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (cat, Q165H)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}
Design 9	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{ALD6}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (cat, N116S)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}
Design 10	LexO-P_{LEU2m}	sfGFP	T_{TDH1}	P_{ALD6}	Gpa1-Gαi3	T_{ENO2}	P_{TDH3}	P2Y2 (cat, F58I)	T_{SSA1}	P_{RAD27}	LexA-PRD	T_{ENO1}

b

Name	Description	Sensitivity	Max output	Operational range	Dynamic range	Tightness
		1/(lowest log concentration for which a >2-fold change in GFP expression)	Maximum fluorescence output	Concentration between the sensitivity and the lowest concentration that gives a GFP output half of the maximum	Maximum output/basal activity	1/basal fluorescence
Design 1	Initial design	NA	375.00	NA	NA	NA
Design 2	LexA-PRD transcription factor	NA	468.56	NA	NA	NA
Design 3	creased Gpa1 chimera express	NA	1918.18	NA	2.16	1.13E-03
Design 4	P2Y2 from mouse	NA	1542.68	NA	2.05	1.33E-03
Design 5	P2Y2 from olive baboon	0.23	12260.93	0.92	18.25	1.49E-03
Design 6	P2Y2 from green monkey	0.19	3569.00	NA	3.15	8.81E-03
Design 7	P2Y2 from cat	0.25	20840.35	0.98	26.83	1.29E-03
Design 8	P2Y2 from cat, Q165H	0.39	17833.95	0.91	6.91	3.88E-03
Design 9	P2Y2 from cat, N116S	0.17	20176.53	NA	1.35	6.71E-03
Design 10	P2Y2 from cat, F58I	0.33	28216.04	1.38	32.96	1.17E-03

Supplementary Fig. 2: Modular circuit layouts and dose-response characteristics of yeast eATP sensor strains.

(**a**) A list of parts and layouts of multigene cassettes for each eATP sensor strain design. The cassettes are integrated at the *URA3* loci. (TF: transcription factor). (**b**) Dose-response characteristics for the yeast eATP sensor strains.

Supplementary Fig. 3: Colon images of mice with indicated treatments on day 12. Control: healthy control group (n=5 mice); DSS-PBS: DSS-induced mice administered PBS (n=10 mice); DSS-WT: DSS-induced mice administered synthetic starter with wild-type yeast and *L. plantarum* (n=11 mice); DSS-TH: DSS-induced mice administered therapeutic SINERGY (n=11 mice).