Supplemental Table 1

P values of the five coupling types in the analyzed networks. The p values are estimated by employing network randomization under mass-balance constraints (Basler et al. *Bioinformatics* 2011 27: 1397-1403), and are derived from a z-score, which is determined from 100 (Ec iJO1366, *H sapiens* recon1, human tissue specific and cancer networks) or 1,000 (remaining networks) randomized networks, respectively. n/a indicates that no such coupling exists in the corresponding network.

Network	Full	Partial	Directional	Anti	Inhibitive
A niger	$3.39 \cdot 10^{-8}$	0.65	$3.71 \cdot 10^{-9}$	n/a	$4.60 \cdot 10^{-15}$
ArabidopsisCoreModel auto	0.24	0.74	0.15	0.14	0.15
C reinhardtii iAM303	$4.42 \cdot 10^{-4}$	0.48	$5.23 \cdot 10^{-4}$	n/a	$2.51 \cdot 10^{-9}$
Ec iJO1366	0.06	0.44	0.12	n/a	0.01
Ecoli Carbon	$3.50 \cdot 10^{-3}$	0.80	0.04	0.91	$3.98 \cdot 10^{-5}$
Ecoli Core	$7.6 \cdot 10^{-3}$	0.70	0.10	n/a	$7.0 \cdot 10^{-3}$
H sapiens recon1	$1.49 \cdot 10^{-7}$	0.30	$1.70 \cdot 10^{-11}$	n/a	$3.67 \cdot 10^{-25}$
M acetivorans iMB745	0.27	0.10	0.11	n/a	0.06
M barkeri iAF692	0.13	0.16	0.35	0.43	0.05
M musculus	$2.70 \cdot 10^{-3}$	0.79	$1.90 \cdot 10^{-3}$	n/a	0.01
M pneumoniae iJW145	$8.30 \cdot 10^{-3}$	0.96	0.02	0	$7.2 \cdot 10^{-3}$
M tuberculosis iNJ661	$4.48 \cdot 10^{-4}$	0.69	$3.87 \cdot 10^{-4}$	n/a	$1.17 \cdot 10^{-5}$
N pharaonis	$1.85 \cdot 10^{-5}$	0.91	$7.38 \cdot 10^{-4}$	n/a	$1.91 \cdot 10^{-4}$
P putida iJN746	$4.86 \cdot 10^{-4}$	0.71	$2.7 \cdot 10^{-3}$	n/a	$9.69 \cdot 10^{-5}$
T maritima	0.31	0.92	0.22	0.42	0.10
BreastHealthy	$1.08 \cdot 10^{-6}$	0.39	$3.74 \cdot 10^{-4}$	n/a	$8.10 \cdot 10^{-30}$
iBreastCancer1771	$7.34 \cdot 10^{-4}$	0.43	$8.7 \cdot 10^{-3}$	n/a	$1.42 \cdot 10^{-7}$
KidneyHealthy	$4.15 \cdot 10^{-6}$	0.29	0.17	n/a	$2.16 \cdot 10^{-6}$
iRenalCancer1410	$4.6 \cdot 10^{-3}$	0.62	$8.8 \cdot 10^{-3}$	n/a	$1.38 \cdot 10^{-5}$
LungHealthy	$3.9 \cdot 10^{-3}$	0.12	$3.6 \cdot 10^{-3}$	n/a	$1.71 \cdot 10^{-16}$
iLungCancer1472	$2.46 \cdot 10^{-4}$	0.46	$3.63 \cdot 10^{-4}$	n/a	$9.64 \cdot 10^{-8}$
UrothelialHealthy	$1.42 \cdot 10^{-4}$	0.46	$2.1 \cdot 10^{-3}$	n/a	$1.17 \cdot 10^{-15}$
iUrothelialCancer1647	$2.20 \cdot 10^{-3}$	0.22	$9.94 \cdot 10^{-7}$	n/a	$1.04 \cdot 10^{-11}$