

**Table S1. *C. neoformans* mutants showing altered interactions with macrophages<sup>a</sup>****A. Increased uptake mutants**

Index <sup>b</sup>	Library well <sup>c</sup>	Gene ID	Gene name <sup>d</sup>	Description and/or functional domains	Reference
2.51	4C6	CNAG_01172	<i>PBX1</i>	Parallel beta-helix repeat protein; surface glycan synthesis/remodeling	Kumar et al., 2014; Liu et al., 2007
2.42	8E6	CNAG_02797	<i>CPL1</i>	Putative secreted protein; capsule synthesis and/or assembly	Cai et al., 2014; Liu et al., 2008
2.25	2G9	CNAG_05431	<i>RIM101</i>	Transcription factor; regulation of cell wall assembly in response to pH	O'Meara et al., 2013; O'Meara et al., 2014
2.11	11A5	CNAG_04514	<i>MPK1</i>	MAP kinase; cell integrity signaling and metabolite resistance	Kraus et al., 2003
2.10	9H11	CNAG_03018	<b>ASG101</b>	Zinc finger transcription factor; homologous to <i>S. cerevisiae</i> <i>ASG1</i>	This study
1.90	2E9	CNAG_00396	<i>PKA1</i>	cAMP dependent protein kinase; mating and virulence signaling	Choi et al., 2012; D'Souza et al., 2001
1.77	12B2	CNAG_01551	<i>GAT201</i>	Transcription factor; regulation of anti-phagocytic mechanisms	Chun et al., 2011; Liu et al., 2008
1.72	1A9	CNAG_06086	<i>CDK8</i>	Cyclin-dependent protein kinase 8	FungiDB
1.50	10D3	CNAG_04863	<i>VPS25</i>	Component of the ESCRT complex; protein sorting/degradation	Chun and Madhani, 2010; Liu et al., 2008
1.43	8F11	CNAG_03188	<i>SET202</i>	Histone-lysine N-methyltransferase	Liu et al., 2008
1.37	7A3	CNAG_01483	<b>HPI1</b>	Ring/zinc finger; similar to E3 ubiquitin ligases	This study
1.34	13H5	CNAG_03409	<i>SKN7</i>	Two-component system response regulator; regulates stress responses	Bahn et al., 2006; Coenjaerts et al., 2006
1.33	9D8	CNAG_04158	<b>HIR1</b>	Nucleosome assembly complex protein, involved in histone gene transcription	This study
1.32	1C12	CNAG_04118	<b>CTK1</b>	CMGC/CDK/CRK7 protein kinase	This study
1.29	2H1	CNAG_00375	<i>GCN5</i>	SAGA complex histone acetyltransferase	O'Meara et al., 2010
1.28	3H6	CNAG_07253	<b>HPI2</b>	Cupin-like domain, conserved in <i>Cryptococcus</i> ; no homologues in <i>S. cerevisiae</i>	This study
1.23	4A7	CNAG_00455	<i>UBP16</i>	ubiquitin carboxyl-terminal hydrolase	FungiDB
1.18	4D3	CNAG_07315	<i>LIV6</i>	CDA08-related protein (T-cell immunomodulatory protein homolog); possibly involved in endosome function	Brown and Madhani, 2012; Liu et al., 2008
1.18	7H1	CNAG_03202	<i>CAC1</i>	Adenylate cyclase	Alspaugh et al., 2002
1.17	1E2	CNAG_06762	<i>GAT204</i>	GATA transcription factor; capsule-independent antiphagocytic protein	Chun et al., 2011; Haynes et al., 2011
1.17	12C1	CNAG_00110	<b>HPI3</b>	Hypothetical protein; no homolog in <i>S. cerevisiae</i>	This study
1.14	12A11	CNAG_05590	<i>TCO2</i>	Two-component-like sensor kinase	Bahn et al., 2006
1.14	2A12	CNAG_03981	<b>PFA4</b>	DHHC protein palmitoyltransferase	This study
1.14	3E10	CNAG_05787	<b>HPI4</b>	Similar to symplekin protein	This study
1.14	3G5	CNAG_00367	<i>DYN5</i>	Dynactin Arp1 p25 subunit	FungiDB

**B. Decreased uptake mutants**

Index <sup>b</sup>	Library well <sup>c</sup>	Gene ID	Gene name <sup>d</sup>	Description and/or functional domains	Reference
-4.05	4H8	CNAG_01964	<i>OPT1</i>	Proton-coupled oligopeptide transporter	FungiDB
-2.71	4C12	CNAG_01640	<b>CSF1</b>	Hypothetical protein; homologous to <i>S. cerevisiae</i> <i>CSF1</i>	This study

-2.56	9B5	CNAG_06759	<b>LPI1</b>	Dehydrogenase	This study
-2.47	5G8	CNAG_07351	<b>LPI2</b>	Hypothetical protein; no homologs in <i>S. cerevisiae</i>	This study
-2.41	4H9	CNAG_06370	<b>BAT2</b>	Branched-chain-amino-acid aminotransferase	FungiDB
-2.21	12D6	CNAG_02580	<b>LPI3</b>	Hypothetical protein; no homologs in <i>S. cerevisiae</i>	This study
-2.01	9E4	CNAG_01262	<b>GPB1</b>	G-protein $\beta$ -subunit involved in pheromone sensing and mating	Wang et al., 2000
-2.01	9A12	CNAG_06074	<b>LPI4</b>	Cytoplasmic protein of unknown function	This study
-2.00	10H11	CNAG_00414	<b>MAK32</b>	Hypothetical protein; homologous to <i>S. cerevisiae</i> MAK32	This study
-1.96	1F6	CNAG_07534	<b>TRS130</b>	Hypothetical protein; homologous to <i>S. cerevisiae</i> TRS130	This study
-1.83	10H1	CNAG_03912	<b>LPI5</b>	Transporter of the major facilitator superfamily	This study
-1.83	9H5	CNAG_04461	<b>HFM1</b>	ATP-dependent DNA helicase	FungiDB
-1.79	2E8	CNAG_04256	<b>LPI6</b>	Hypothetical protein; no homologs in <i>S. cerevisiae</i>	This study
-1.78	12F2	CNAG_07580	<b>LPI7</b>	CAMK protein kinase; domains typical of serine/threonine kinases but also methyltransferases and DNA binding	This study
-1.77	7G5	CNAG_06986	<b>LPI8</b>	Sugar transporter	This study
-1.71	9G10	CNAG_05411	<b>LPI9</b>	Endoglucanase	This study
-1.63	10H4	CNAG_04546	<b>LPI10</b>	Multidrug transporter	This study
-1.63	10E9	CNAG_00745	<b>HRK1</b>	Serine/threonine-protein kinase	Kim et al., 2011
-1.62	12D3	CNAG_05077	<b>LPI11</b>	Glycosyl hydrolase	This study
-1.59	4F3	CNAG_07180	<b>SIR2</b>	NAD-dependent histone deacetylase	FungiDB
-1.58	7H6	CNAG_02581	<b>CAS33</b>	Capsular associated protein; involved in modification of GXM polysaccharide	Moyrand et al., 2004
-1.57	9D5	CNAG_02254	<b>LPI12</b>	Transporter of the major facilitator superfamily; similar to quinate permeases	This study
-1.53	6H4	CNAG_00387	<b>LPI13</b>	Hypothetical protein; domains typical of GTPase activating proteins	This study
-1.51	4A12	CNAG_04681	<b>LPI14</b>	Hypothetical transmembrane protein; no homologs in <i>S. cerevisiae</i>	This study
-1.47	9D2	CNAG_00699	<b>LPI15</b>	Membrane protein; domains typical of WSC proteins, polycystin, and fungal exoglucanase	This study
-1.44	6G4	CNAG_05468	<b>APN1</b>	Apurinic/aprimidinic endonuclease; homologous to <i>S. cerevisiae</i> APN1	This study
-1.44	7D9	CNAG_00353	<b>LPI16</b>	3-oxo-5- $\alpha$ -steroid 4-dehydrogenase (steroid reductase)	This study
-1.44	1D5	CNAG_07422	<b>DHA1</b>	Glycoprotein that elicits a delayed-type hypersensitivity response in mice	Mandel et al., 2000
-1.43	6G8	CNAG_02941	<b>LPI17</b>	Hypothetical protein; no homologs in <i>S. cerevisiae</i>	This study
-1.42	1E6	CNAG_06290	<b>SNF3/ HXT2<sup>e</sup></b>	Low-affinity glucose (hexose) transporter	Liu et al., 2013

<sup>a</sup> All 56 mutants identified in the screen, listed by increased (A) or decreased (B) phagocytic index.

<sup>b</sup> Value shown is the average (on a binary log scale) of the adjusted uptake of each strain from three independent screens.

<sup>c</sup> Location of the strain in the deletion collection (see Liu et al., 2008).

<sup>d</sup> Bold indicates new names given to uncharacterized genes either based on homology to *S. cerevisiae* per nomenclature guidelines (see Inglis et al., 2014) or, for genes with no homology to *S. cerevisiae*, based on phenotype: *HPI* or *LPI* mutants, for High or Low Phagocytic Index.

<sup>e</sup> Gene CNAG\_06290 appears in fungal databases as *SNF3* but was published as *HXT2* (Liu et al., 2013).

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