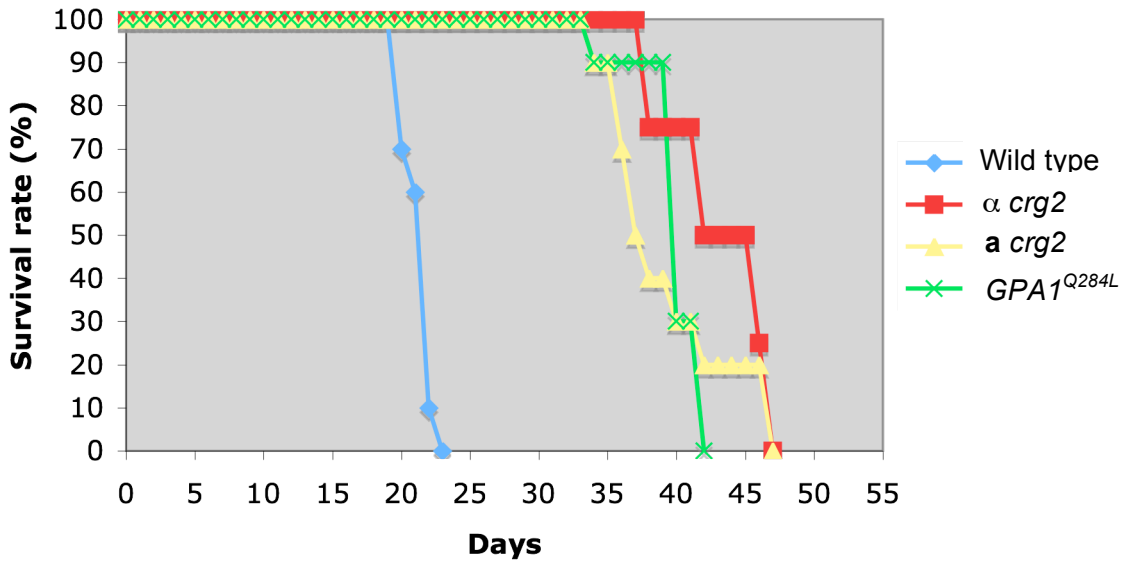
Supplemental Table 1. Primers used in this study

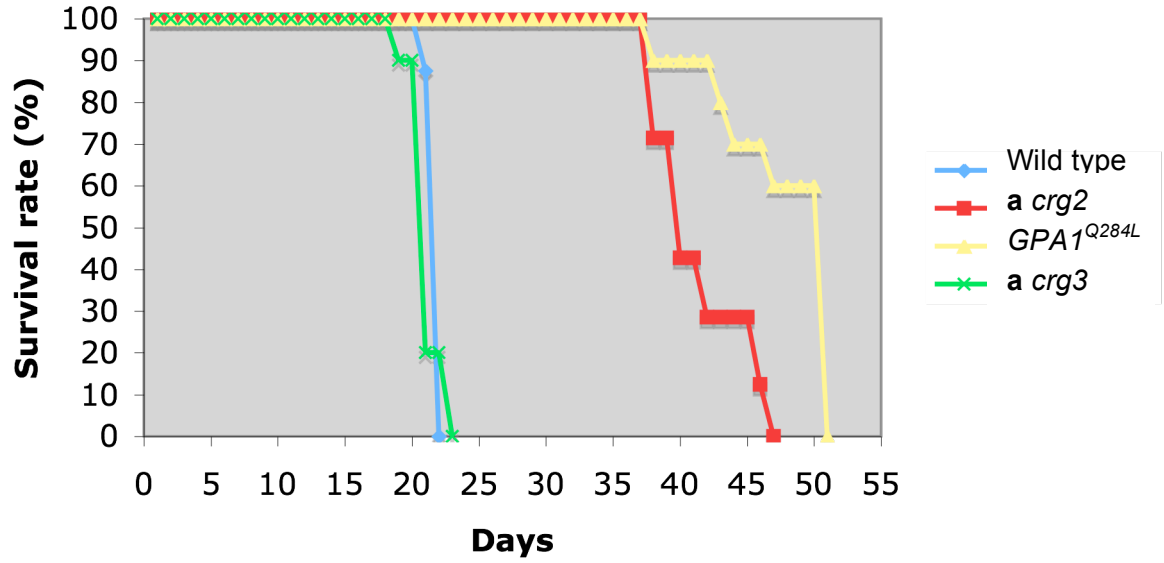
Primer name	Sequence (5' – 3')
M13F	GTAAAACGACGGCCAG
M13R	CAGGAAACAGCTATGAC
JH12497	GGCCCGGGATGGGCGGCTGTATGTCTACTCCAGAAG
JH12498	GGCCCGGGAACTATCCGCCAGTCAGACAGGAG
JH12499	CATTCATATGTTCGATGTCGGTGGACTGAGAAGCGAGAGAAAGAAGTGG
JH12500	CCACTTCTTTCTCTCGCTTCTCAGTCCACCGACATCGAACATATGAATG
JH13272	TTCAGGCTGCGCAACTGTTG
JH14774	AAGAGATCCCGCAAGAGATCTTC
JH14775	CCGACAACGCTACGGTGATGAC
JH14776	CTGGCCGTCGTTTTACCATGTTGGCATGCCCATGAGCTG
JH14777	GTCATAGCTGTTTCCTGGAACACAGTCATCGTCGTGAAG
JH14778	GTTGAGTGAGTCGCCTTACGCATG
JH14779	CCTTACAGGAGGTACTGGACAG
JH14780	GCGACTAATCTGACAATGCTTC
JH14786	GTCACTCGCTCTCGCTGCCTTG
JH14787	CCTCCCGAGAGTTCGACAATC
JH14788	TTTCTGCACAATATTTCAAGC
JH14789	CTTGACGAAAATCTGCATGG
JH14790	TGGCATGCATGTGCTCTG
JH14791	GTAAGGTGGACTCCTTCT
JH17098	GACTGGATCCGAATGGCAGAAAGCAACGAGAAG
JH17099	GATCCTGCAGATCTACAGTCTCTGACCGGGGAC
JH17832	GGACTGGGTAAGTTTCTTCCTG
JH17833	CTGGCCGTCGTTTTACGTGGAACGCAATGCGAATGTAG
JH18001	GTACGGCCGGCCATGGCAGAAAGCAACGAGAAG
JH18002	GCATTTAATTAACTACAGTCTCTGACCGGGGAC
JH18786	GTACGGCCGGCCGGCCATTACGGCCAGATGGCAGAAAGCAACGAGAAG
JH18787	GCATTTAATTAAGGCCGAGGCGGCCACCTACAGTCTCTGACCGGGGAC
JH18831	CTGTCCAGTACCTCCTGTAAGG
JH18832	CCTGCAATGTCTCTGAAACCAC
JH18838	GATCCTGCAGATTTACAGGGGAGTAAGATTGGCAAAG
JH19001	GACTCCCGGGTATGGGCGGCTGTATGTCTACTC
JH19002	GATCCTCGAGTTATAAGATACCAGAGTCACGTAAAG
JH20163	GCTTTCAGCGTAATCTAGTCTATTACAG GGGAGTAAGATTGGCAAAG

JH20164	CTTTGCCAATCTTACTCCCCTGTAATAGACTAGATTACGCTGAAAGC
JH20165	TCTAGTCTA TTA GAGGACGACGCACAGGGGAGTAAGATTGGCAAAG
JH20166	ACTCCCCTG TGCGTCGTCCTC TAA TAGACTAGATTACGCTGAAAGC
JH20181	GTCATAGCTGTTTCCTGCATGATTACGCCAAGCTTGCATG

A



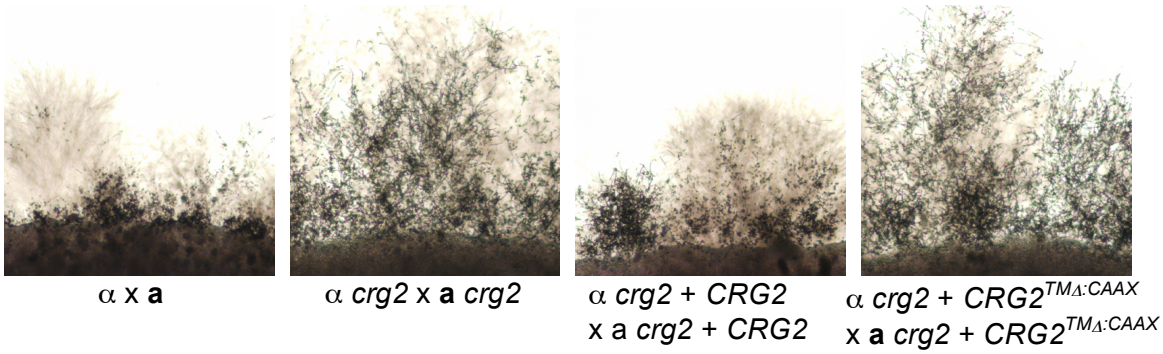
B



Supplemental Figure S1. Crg2 regulates virulence in a murine inhalation model.

Female A/Jcr mice were intranasally inoculated with 10^5 cells of the following strains in two separate experiements: (A) wild type (H99), α *crg2* mutant 1 (CDX50), **a** *crg2* mutant 2 (CDX51), *GPA1*^{Q284L} strain 2 (CDX156-4); (B) wild type (H99), **a** *crg2* mutant 3 (CDX111), *GPA1*^{Q284L} strain 3 (CDX40), and *crg3* mutant (CDX53). Animals were

monitored for clinical signs of cryptococcal infection and sacrificed at predetermined clinical end points that predict imminent mortality. All *crg2* mutants and *GPA1*^{Q284L} strains tested showed significantly reduced virulence compared to the wild type strain H99 ($P<0.001$) based on the PRISM 4 program 4.0 (Graph Software, San Diego, CA).



Supplementary Figure S2: Function of transmembrane domains in sexual reproduction of Crg2 protein. Bilateral matings for the following strains were performed on V8 medium: wild type (H99 and KN99**a**), *crg2* (CDX50 and CDX51), *crg2* + *CRG2* (CDX180 and CDX181), α *crg2* + *CRG2*$^{TM\Delta:CAAX}$ (CDX184 and CDX185). Mating results on V8 medium were photographed after 10 days of incubation in the dark at 25°C.