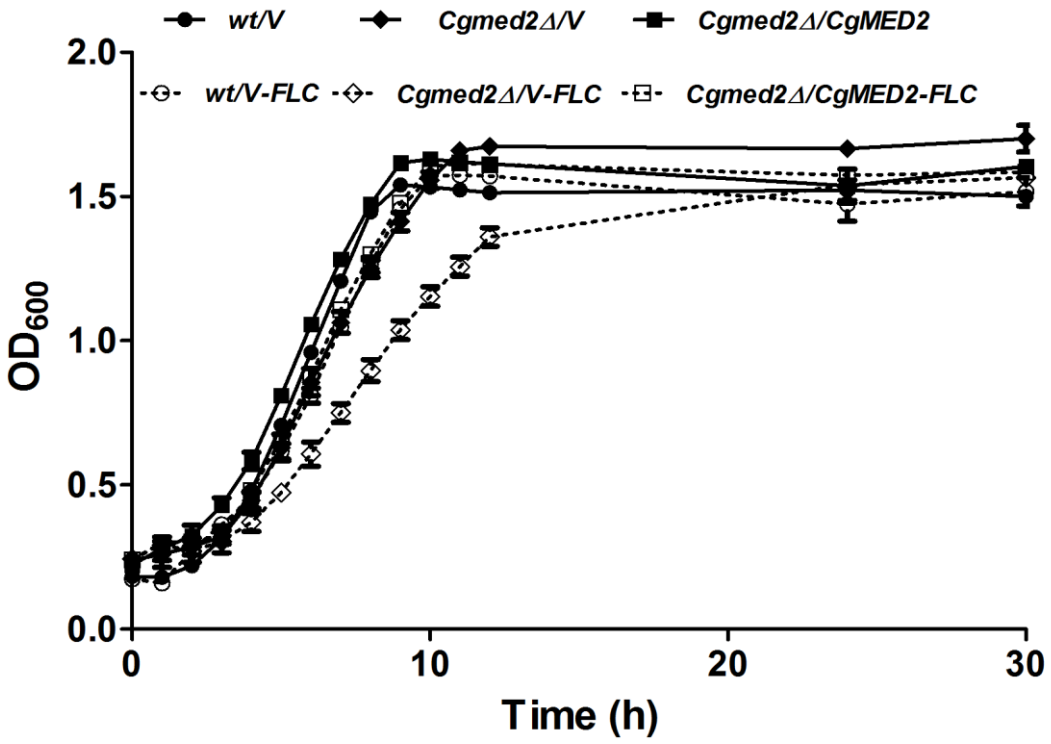

Figure S1. Disruption of the *CgMED2* gene leads to increased susceptibility to fluconazole.

Growth profile analysis of indicated *C. glabrata* strains in the YPD medium containing or lacking 16 μg/ml fluconazole (FLC 16) at 30°C. Data represent the means from three independent growth analyses ± SEM. Solid and dotted lines indicate untreated and fluconazole-treated cultures, respectively.

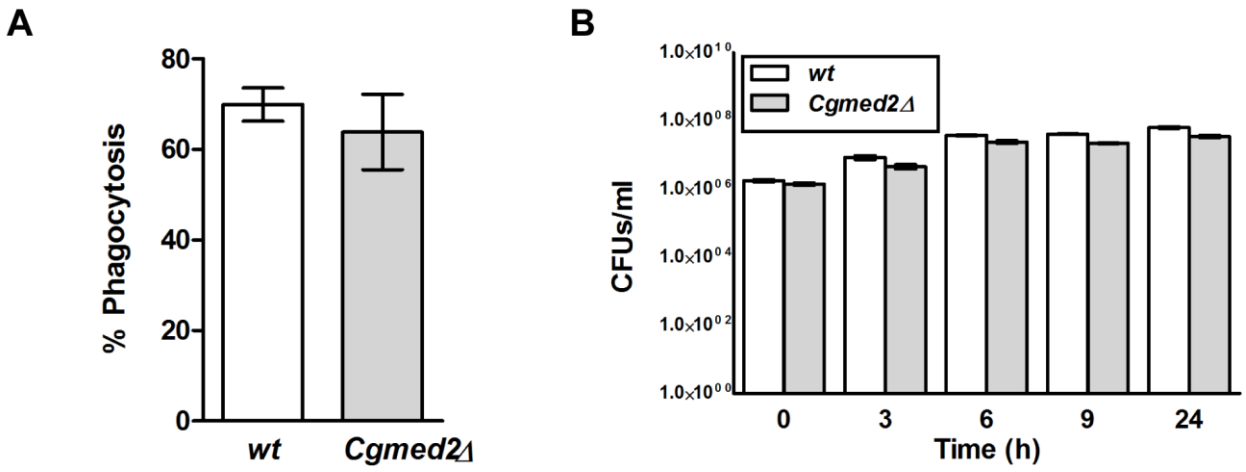

Figure S2. Disruption of the *CgMED2* gene does not affect the uptake of *C. glabrata* cells by THP-1 macrophages.

A. *wt* and the *Cgmed2*Δcells were infected to THP-1 macrophages at a MOI of 1:10. After 2 h coincubation, extracellular *C. glabrata* cells were washed off with three PBS washes and the number of intracellular yeast cells was determined by plating appropriate dilutions of macrophage lysates on YPD medium. % phagocytosis rate was calculated by dividing the number of intracellular yeast cells 2 h post infection to the number of yeast cells infected to THP-1 macropahges. Data represent means±SEM of three independent infection experiments.

B. *wt* and the *Cgmed2*Δ cells were grown in RPMI medium for indicated time periods and growth was recorded by plating appropriate culture dilutions on YPD medium and counting the total number of CFUs.

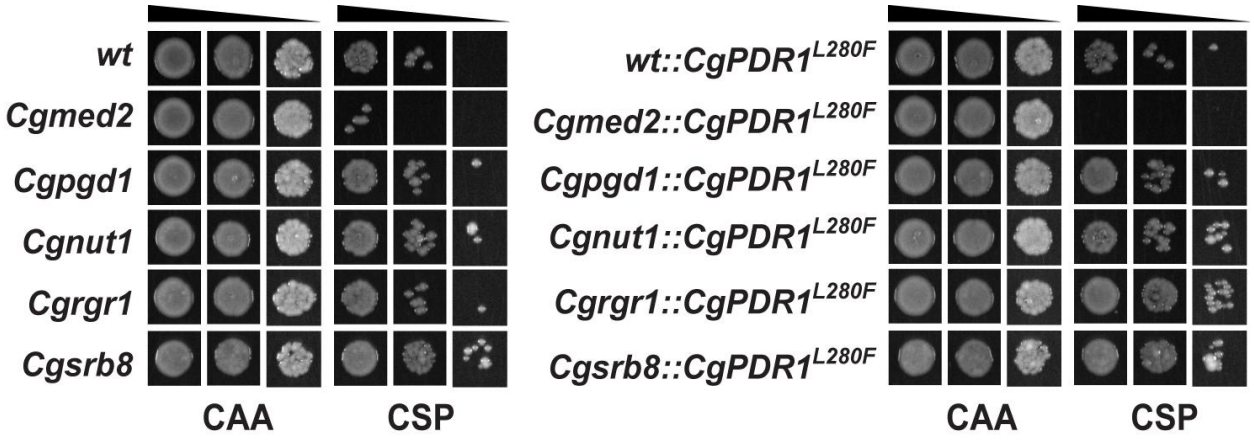

Figure S3. The *Cgmed2*Δ mutant exhibits sensitivity to caspofungin. *wt* and *Cgmed2*Δ cells were grown in CAA medium lacking or containing 0.05 μg/ml caspofungin for 24 h, diluted 10-, 100- and 1000-fold in PBS and 3 μl of each culture dilution was spotted on YPD medium. Growth was recorded after 24 h.

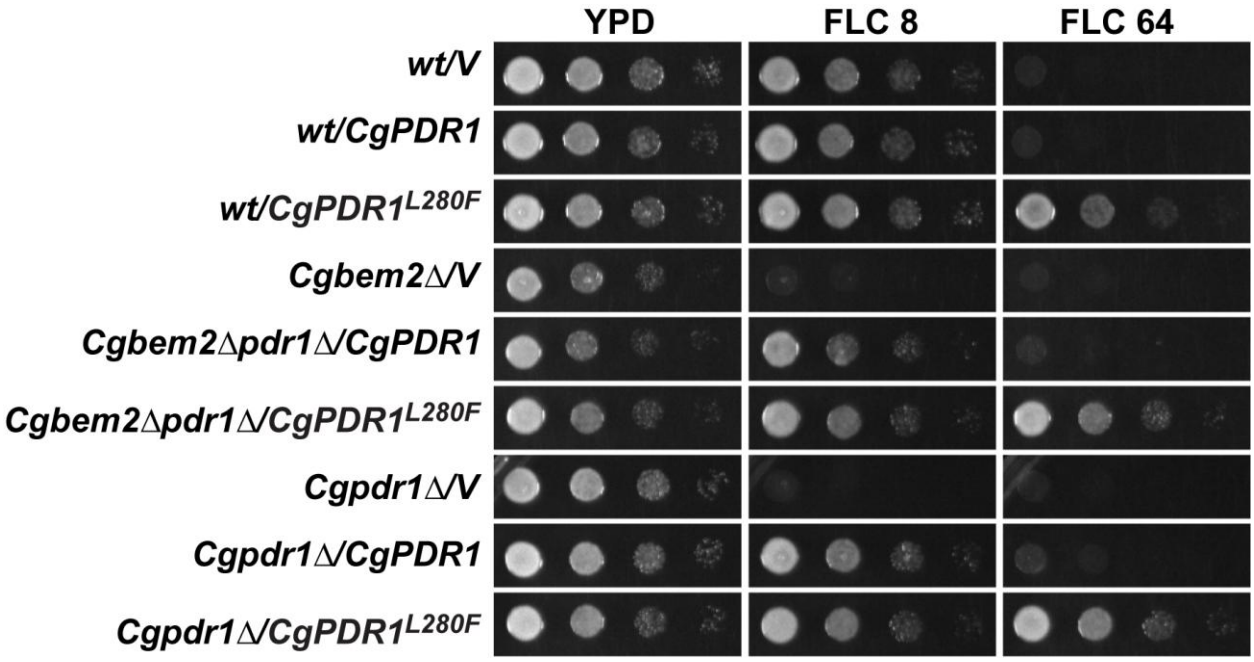

Figure S4. Expression of the GOF *CgPDR1* allele conferred fluconazole resistance in *Cgbem2*Δ cells.

Serial dilution spot assay of indicated *C. glabrata* strains on YPD and YPD medium containing8 (FLC 8) and 64 μg/ml (FLC 64) fluconazole. The *Cgpdr1*Δ mutant was used as a control. Expression of the wild-type *CgPDR1* allele complemented the fluconazole sensitivity of the *Cgpdr1*Δ mutant while expression of the GOF *CgPDR1*^{L280F}allele rendered the mutant hyper-resistant to fluconazole. Plates were imaged after 1 day of incubation at 30˚C.

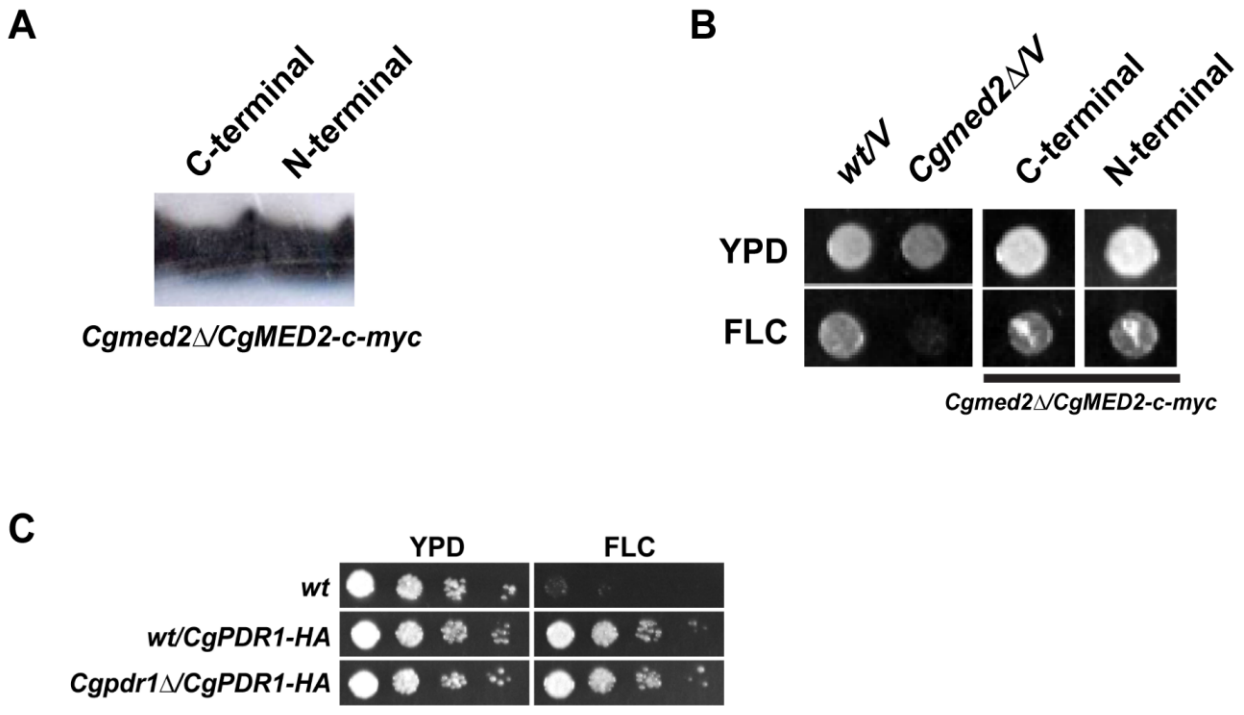

Figure S5. N- and C-terminally-myc-tagged CgMed2 could rescue the fluconazole sensitivity of the *Cgmed2*Δ mutant.

A. Representative Western blot analysis for expression of N- and C-terminally-myc-tagged CgMed2protein in log-phase *wt* cells.Protein extracts were resolved on a SDS-12% PAGE and immunoblotted with the polyclonal antibody against the myc-tag (Sigma-Aldrich # C3956).

B. Serial dilution spot assay of indicated *C. glabrata* transformants on YPD and YPD medium containing 8 μg/ml fluconazole (FLC). Plates were imaged after 1 day of incubation at 30°C.

C. Serial dilution spot assay of indicated *C. glabrata* transformants on YPD and YPD medium containing 32 μg/ml (FLC) fluconazole. Plates were imaged after 1 day of incubation at 30°C.

Table S1: List of strains and plasmids used in the study

Strain	Relevant genotype	Reference
Yeast		
BG2	Clinical isolate	Fidel *et al*., 1996
YRK19	*ura3*Δ*::Tn903 G418*^{R}	Cormack and Falkow, 1999
YRK20	*URA3*	De Las Peñas *et al*., 2003
YRK527	*ura3*Δ*::Tn903 G418*^{R}*Cgbem2*Δ*::nat1*	Borah *et al*., 2011
YRK747	*Cgmed2*Δ*::nat1*	This study
YRK758	*ura3*Δ*::Tn903 G418*^{R}*Cgmed2*Δ*::nat1*	This study
YRK798	YRK758/pBRK74	This study
YRK799	YRK758/pBRK1021	This study
YRK809	*ura3*Δ*::Tn903 G418*^{R}*Cgpdr1*Δ*::nat1*	This study
YRK810	*ura3*Δ*::Tn903 G418*^{R}*Cgbem2*Δ*Cgpdr1*Δ*::nat1*	This study
YRK812	YRK809/pBRK943 (*Cgpdr1*Δ*/V*)	This study
YRK813	YRK809/pBRK945 (*Cgpdr1*Δ*/CgPDR1*)	This study
YRK814	YRK809/pBRK946 (*Cgpdr1*Δ*/Cgpdr1*^{L280F})	This study
YRK815	YRK810/pBRK943 (*Cgbem2*Δ*Cgpdr1*Δ*/V*)	This study
YRK816	YRK810/pBRK945 (*Cgbem2*Δ*Cgpdr1*Δ*/CgPDR1*)	This study
YRK817	YRK810/pBRK946 (*Cgbem2*Δ*Cgpdr1*Δ*/Cgpdr1*^{L280F})	This study
YRK821	YRK19/pBRK943 (*wt/V)*	This study
YRK822	YRK19/pBRK945 (*wt/CgPDR1)*	This study
YRK823	YRK19/pBRK946 (*wt/Cgpdr1*^{L280F}*)*	This study
YRK835	YRK758/pBRK943 (*Cgmed2*Δ*/V)*	This study
YRK836	YRK758/pBRK945 (*Cgmed2*Δ*/CgPDR1*)	This study
YRK837	YRK758/pBRK946 (*Cgmed2*Δ*/ Cgpdr1*^{L280F})	This study
YRK858	YRK758/pBRK961(*Cgmed2*Δ*/CgMED2-c-myc)*	This study
YRK859	YRK758/pBRK963 (*Cgmed2*Δ*/CgMED2-c-myc)*	This study
YRK1130	YRK19/*CgPDR1-HA*	This study
YRK1131	YRK809/*CgPDR1-HA*	This study
Transposon		
Tn7	Tn*7* R6Kγori *URA3 npt* (Km^{R})	Castaño *et al*., 2003
YRK673	*Cgmed2*Δ*::Tn7*	Borah *et al*., 2011
YRK675	*Cgpgd1*Δ*::Tn7*	Borah *et al*., 2011
YRK943	*Cgnut1*Δ*::Tn7*	Kaur *et al*., 2004
YRK945	*Cgrgr1*Δ*::Tn7*	Kaur *et al*., 2004
YRK947	*Cgsrb8*Δ*::Tn7*	Kaur *et al*., 2004
YRK1011	*wt::Cgpdr1*^{L280F}	This study
YRK1012	*Cgmed2*Δ*::Tn7::Cgpdr1*^{L280F}	This study
YRK1014	*Cgpgd1*Δ*::Tn7::Cgpdr1*^{L280F}	This study
YRK1015	*Cgrgr1*Δ*::Tn7::Cgpdr1*^{L280F}	This study
YRK1016	*Cgnut1*Δ*::Tn7::Cgpdr1*^{L280F}	This study

YRK1017	*Cgsrb8Δ::Tn7::Cgpdr1*^{L280F}	This study
Plasmid	**Description**	**Reference**
pRK74	CEN-ARS plasmid (pGRB2.2) of C. *glabrata* carrying S. *cerevisiae URA3* as a selection marker. MCS sites are flanked by *S. cerevisiae PGK1* promoter at one end and by 3' UTR of *HIS3* at the other end	Frieman *et al*., 2002
pBRK943	CEN-ARS vector pCgACU5	Sanglard laboratory
pBRK945	pSF4, pCgACU5-derived plasmid containing *CgPDR1* from wild-type strain	Sanglard laboratory
pBRK946	pSF5, pCgACU5-derived plasmid containing *CgPDR1* from azole resistant strain (DSY565)	Sanglard laboratory
pBRK947	pSF2, *CgPDR1* deletion plasmid, *SAT1-FLIP* marker	Sanglard laboratory
pBRK949	pSF67, plasmid with *CgPDR1* hyperactive allele (DSY565)	Sanglard laboratory
pBRK961	*CgMED2* tagged with c-myc at C-terminal	This study
pBRK963	*CgMED2* tagged with c-myc at N-terminal	This study
pBRK1021	*CgMED2* (*CAGL0C04477g*) cloned into pRK74 plasmid	This study

Table S2: List of primers used in the study

Primer	Sequence	Details	Reference
Primers for generation of *Cgmed2*Δdeletion strain			
OgRK801	GTATCATCGGGGGTTGTGAC	*CgMED2* 5' UTR Forward	This study
OgRK802	GCGTCGACCTGCAGCGTACGAAAGACCCAGTGTTCGCAGT	*CgMED2* 5' UTR Reverse	This study
OgRK803	CGACGGTGTCGGTCTCGTAGAAAGTTTGAAAGTGTTTTACCTTGTG	*CgMED2* 3' UTR Forward	This study
OgRK804	ATGGGATGTCATAGACGATCAA	*CgMED2* 3' UTR Reverse	This study
OgRK805	CGGGTACCCATATTTCGATG	*CgMED2* 5' integration check Forward	This study
OgRK806	TTGCTCAGCATGTTCTCCAG	*CgMED2* 5' integration check Reverse	This study
OgRK807	AATCCATCTGCCATGCTAGG	*CgMED2* 3' integration check Forward	This study
OgRK808	TGCAAAGAGTCGAGAAAGCA	*CgMED2* 3' integration check Reverse	This study
OgRK809	AATCCATCTGCCATGCTAGG	*CgMED2*internal Forward	This study
OgRK810	GTCTAGGTCACCGCCTTCAC	*CgMED2*internal Reverse	This study
Primers for cloning			
OgRK843	GAGACCCGGGGCGAACACTGGGTCTTTTT	*CgMED2* Forward	This study
OgRK844	GAGGTCGACGCATTTAGATATTAAAGCCATTTAGG	*CgMED2* Reverse	This study
OgRK1143	GAGACCCGGGTGGAACAAAAACTTATTTCTGAAGAAGATCTGAGTTACAAGAACAGGCTTAC	*CgMED2-c-myc* Forward	This study
OgRK1144	GAGGTCGACTTACAGATCTTCTTCAGAAATAAGTTTTTGTTCGATATTAAAGCCATTTAGG	*CgMED2-c-myc* Reverse	This study
OgRK1179	CCGGATCCAATATGCAAACATTAGAAACTACATCA	*CgPDR1-HA* Forward	This study
OgRK1182	CGCCCCGGGTTAAGCGTAGTCTGGGACGTCGTATGGGTACAAGTAAACATCAGAAA	*CgPDR1-HA* Reverse	This study
Primers for qRT-PCR			

OgRK127	TGCAGGACCAAGTCAGACAG	*CgCDR1* Forward	Borah *et al*.,2011
OgRK128	CTCATCGGAAGTAGGGTCCA	*CgCDR1* Reverse	Borah *et al*.,2011
OgRK133	ACGGTACCAAGCCATACGAG	*CgERG11* Forward	Borah *et al*.,2011
OgRK134	GAACACTGGGGTGGTCAAGT	*CgERG11* Reverse	Borah *et al*.,2011
OgRK135	AAAGGGAGTGACAGCGAGAA	*CgPDR1* Forward	Borah *et al*.,2011
OgRK136	CTCAATGGCGTCAATGGATGA	*CgPDR1* Reverse	Borah *et al*.,2011
OgRK191	TTTCAGAGTGCCAACTGTCG	*CgTDH3* Forward	Borah *et al*.,2011
OgRK192	TGAAACAACAGCGTCCTCAG	*CgTDH3* Reverse	Borah *et al*.,2011
OgRK1183	ACTATGTTACTTTATGGTTA	*CgEPA1* Forward	This study
OgRK1184	TGAGCCCCAGATGGCGTAGG	*CgEPA1* Reverse	This study
OgRK1592	CCGAATTAGATCATTTACCGG	*CgEPA7* Forward	Iraqui*et al*.,2005
OgRK1593	GAAGGAGTACTATTGGTGATCG	*CgEPA7* Reverse	Iraqui*et al*.,2005

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