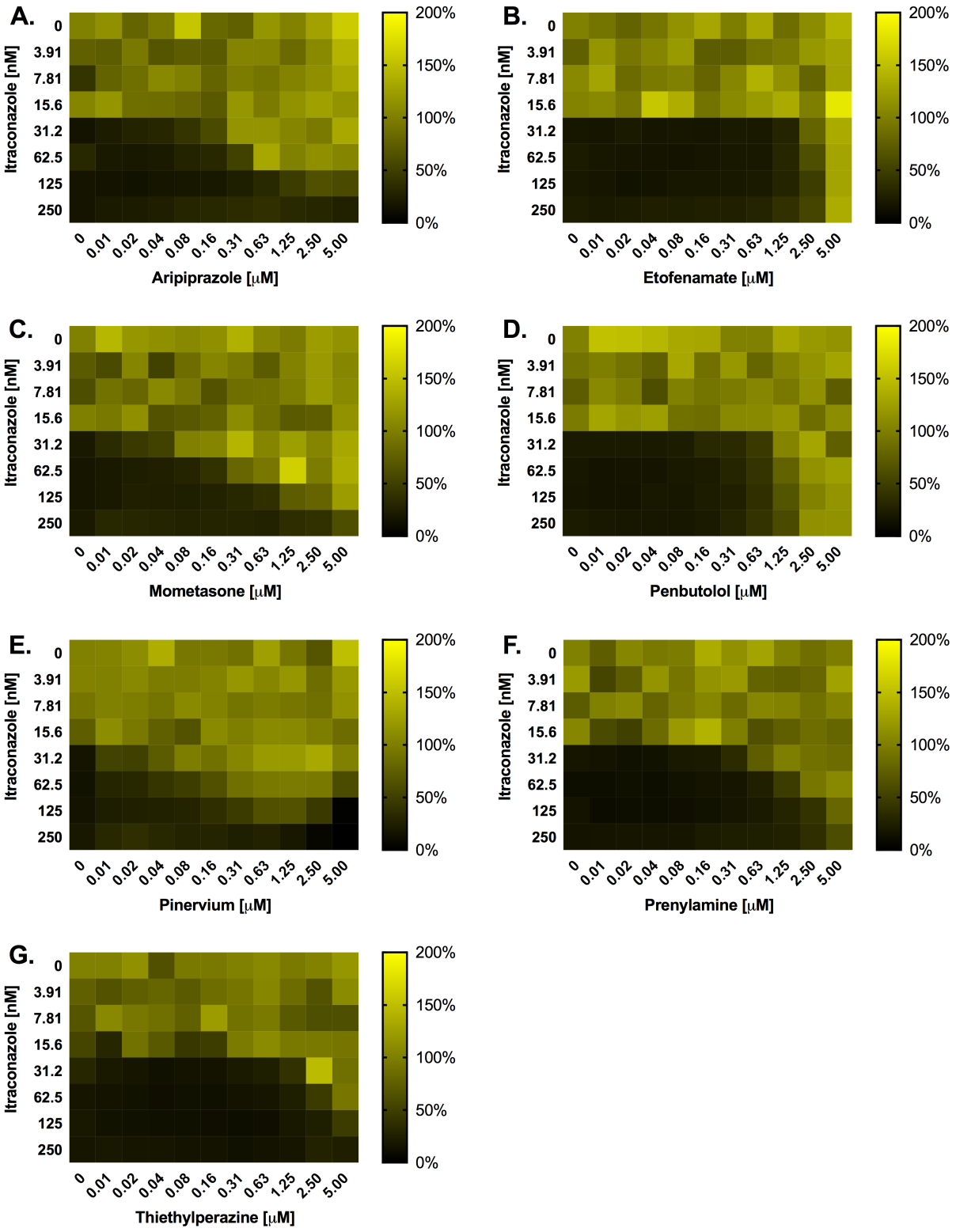
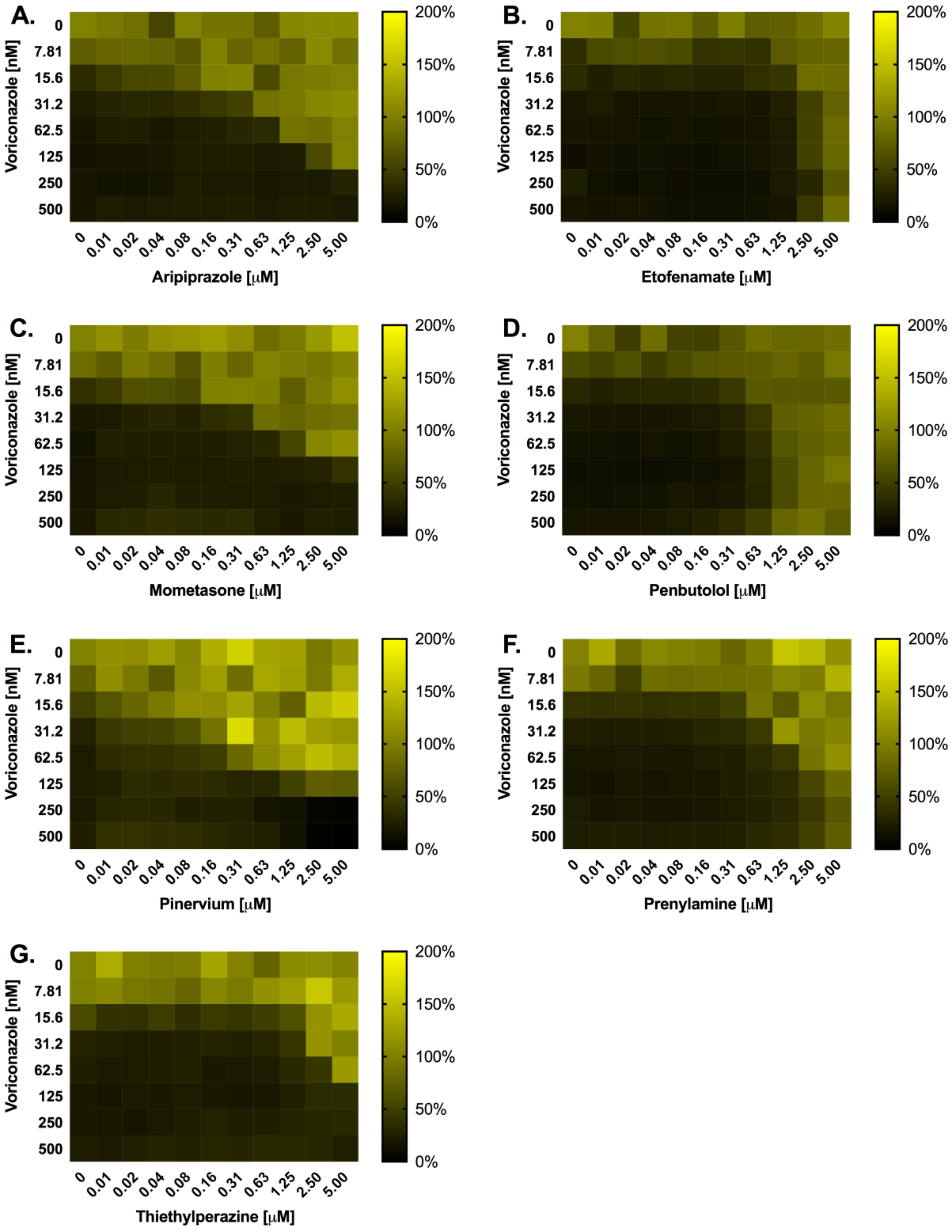


Supplemental Figure 1. A variety of approved medications substantially diminish *Candida albicans* susceptibility to itraconazole. *C. albicans* (strain SC5314) susceptibility to itraconazole was tested in the absence (DMSO vehicle alone) or presence of 5 μM of the indicated compounds, in RPMI medium according to the CLSI broth microdilution protocol. Growth was quantified as OD_{600nm} after 24 hours incubation at 35°C and are presented as percent growth relative to the drug free control. Data from a single experiment representative of two biological replicates is shown.



Supplemental Figure 2. A variety of approved medications substantially diminish *Candida albicans* susceptibility to voriconazole. *C. albicans* (strain SC5314) susceptibility to voriconazole was tested in the absence (DMSO vehicle alone) or presence of 5 μM of the indicated compounds, in RPMI medium according to the CLSI broth microdilution protocol. Growth was quantified as OD_{600nm} after 24 hours incubation at 35°C and are presented as percent growth relative to the drug free control. Data from a single experiment representative of two biological replicates is shown.

Supplemental table 1: Minimum inhibitory concentrations for the selected antifungals under screening conditions with the selected strains. The susceptibility of *C. albicans* strain SC5314, *C. glabrata* strain ATCC2001, *C. tropicalis* strains MYA-3404 or Ct8, and *C. parapsilosis* strain CDC317, to the indicated antifungal drugs was determined according to the CLSI broth microdilution method.

Antifungal	Species	MIC
Fluconazole	*C. albicans*	0.63 μM
	C. parapsilosis	6.25 μM
	C. tropicalis Ct 8	0.39 μM
	C. glabrata	25 μM
Caspofungin	*C. albicans*	125 nM
	C. parapsilosis	250 nM
	C. tropicalis	250 nM
	C. glabrata	125 nM
Amphotericin B	*C. albicans*	125 nM
	C. parapsilosis	250 nM
	C. tropicalis	125 nM
	C. glabrata	250 nM

Supplemental Table 2: Agents from the Prestwick collection that suppress the antifungal activity of fluconazole at 1 μM in *Candida albicans*. The Prestwick collection, containing a variety of FDA-approved drugs was screened with each compound at a final concentration of 5 μM, to identify those which restore the growth of *C. albicans* strain SC5314 in the presence of 1 μM fluconazole (approximately 2-fold MIC). Hits were defined as compounds that restore fungal growth to at least 50% of the untreated control wells.

Screen	Compound	Growth restoration (%)
C. albicans, 1 μM fluconazole	**Untreated**	**100**
	Fluconazole alone	**0**
	Niclosamide	69
	Trifluprom azine hydrochloride	111
	Chlorpromazine hydrochloride	82
	Dibucaine	77

Thioridazine hydrochloride	83
Perphenazine	71
Terfenadine	112
Tamoxifen citrate	68
Nicergoline	56
Asenapine maleate	112
Clemizole hydrochloride	56
Dyclonine hydrochloride	76
Fendiline hydrochloride	116
Pimozide	64
Mebeverine hydrochloride	99
Trifluoperazine dihydrochloride	117
Fluphenazine dihydrochloride	119
Chlorprothixene hydrochloride	110
Metergoline	125
Benfluorex	77
Bepridil hydrochloride	92
Benzbromarone	102
Methiothepin maleate	119
Nefazodone hydrochloride	89
GBR 12909 dihydrochloride	147
Clomiphene citrate	126
Prochlorperazine dimaleate	85
Testosterone propionate	83
Amiodarone hydrochloride	113
Suloctidil	127
Zotepine	65
Progesterone	66
Daunorubicin hydrochloride	67
Metixene hydrochloride	126
Propafenone hydrochloride	69
Fluoxetine hydrochloride	77
Atovaquone	61
Parthenolide	105
Hexetidine	129
DO 897/99	117
Prenylamine lactate	123
Mometasone furoate	109

Azelastine hydrochloride	154
Etofenamate	102
Dimethisoquin hydrochloride	163
Sertindole	90
Pinaverium bromide	128
Proadifen hydrochloride	68
Drofenine hydrochloride	105
Cloperastine hydrochloride	86
Methotrimeprazine maleat salt	68
Auranofin	100
Paroxetine Hydrochloride	101
Beclomethasone dipropionate	61
Promethazine hydrochloride	103
Fluspirilen	105
Toremifene	116
Megestrol acetate	82
Indatraline hydrochloride	97
Naftopidil dihydrochloride	72
Nandrolone	54
Norgestimate	51
Chlormadinone acetate	88
Zuclopenthixol dihydrochloride	89
Deptropine citrate	51
Sertraline	135
Halofantrine hydrochloride	141
Nomegestrol acetate	109
Naftifine hydrochloride	97
Thiethylperazine dimalate	106
Cyproterone acetate	121
Toltrazuril	111
Parbendazole	80
Melengestrol acetate	80
Carvedilol	80
Aripiprazole	128
Ethinylestradiol	65
Aripiprazole	118
Ethinylestradiol	63
(R)-Duloxetine hydrochloride	93
1,8-Dihydroxyanthraquinone	54

	Nitazoxanide	85
	Lofepramine	71
	Epirubicin hydrochloride	92
	Lomerizine hydrochloride	103
	Oxymetholone	87
	Triclabendazole	94

Supplemental Table 3: Agents from the Prestwick collection that suppress the antifungal activity of fluconazole at 25 μM in *Candida parapsilosis*. The Prestwick collection, containing a variety of FDA-approved drugs was screened with each compound at a final concentration of 5 μM, to identify those which restore the growth of a *C. parapsilosis* clinical isolate in the presence of 25 μM fluconazole (approximately 4-fold MIC). Hits were defined as compounds that restore fungal growth to at least 50% of the untreated control wells.

Screen	Compound	Growth restoration (%)
C. parapsilosis, 25 μM fluconazole	**Untreated**	**100**
	Fluconazole alone	**0**
	Trifluprомazine hydrochloride	58
	Chlorpromazine hrydochloride	56
	Thioridazine hydrochloride	61
	Disulfiram	53
	Cyproheptadine hydrochloride	54
	Perphenazine	61
	Perhexiline maleate	55
	Mebeverine hydrochloride	55
	Trifluorperazine dihydrochloride	66
	Fluphenazine dihydrochloride	70
	Maprotiline hydrochloride	56
	Chlorprothixene hydrochloride	64
	Metergoline	57
	Methiothepin maleate	63
	Clomiphene citrate	66
	Prochlorperazine dimaleate	65
	Amiodarone hydrochloride	52
	Zotepine	61
	Hexetidine	59
	Dimethisoquin hydrochloride	66
	Sertindole	52
	Pinaverium bromide	51

	Proadifen hydrochloride	52
	Zuclopenthixol dihrydrochloride	60
	Deptropine citrate	53
	Halofantrine hydrochloride	58
	Penbutolol sulfate	57
	Thiethylperazine dimalate	54
	Nelfinavir mesylate	53

Supplemental Table 4: Agents from the Prestwick collection that suppress the antifungal activity of fluconazole at 1.6 µM in *Candida tropicalis*. The Prestwick collection, containing a variety of FDA-approved drugs was screened with each compound at a final concentration of 5 µM, to identify those which restore the growth of *C. tropicalis* strain Ct8 in the presence of 1.6 µM fluconazole (approximately 4-fold MIC). Hits were defined as compounds that restore fungal growth to at least 50% of the untreated control wells.

Screen	Compound	Growth restoration (%)
C. tropicalis 1.6 µM fluconazole	**Untreated**	**100**
	Fluconazole alone	**0**
	Pyrimethamine	98
	Triflupromazine hydrochloride	95
	Chlorpromazine hydrochloride	85
	Imipramine hydrochloride	50
	Amitryptiline hydrochloride	65
	Thioridazine hydrochloride	100
	Cyproheptadine hydrochloride	75
	Perphenazine	88
	Hydroxyzine dihydrochloride	59
	Astemizole	61
	Tamoxifen citrate	80
	Nicergoline	60
	Alverine citrate	87
	Asenapine maleate	51
	Fenbendazole	54
	Carmofur	74
	Albendazole	67
	Vinpocetine	100
	Clomipramine hydrochloride	94
	Fendiline hydrochloride	72
	Cinnarizine	85

Homochlorocyclizine dihydrochloride	97
Perhexiline maleate	86
Oxybutynin chloride	118
Pimethixene maleate	81
Benzydamine hydrochloride	60
Clemastine fumarate	109
Pimozide	100
Flunarizine dihydrochloride	97
Trifluoperazine dihydrochloride	85
Fluphenazine dihydrochloride	89
Chlorprothixene hydrochloride	105
Benfluorex	107
Bepridil hydrochloride	104
Benzbromarone	83
Methiothepin maleate	72
Clofazimine	71
Nefazodone hydrochloride	98
Lidoflazine	92
GBR 12909 dihydrochloride	107
Carbetapentane citrate	88
Clomiphene citrate	76
Prochlorperazine dimaleate	125
Amiodarone hydrochloride	84
Zotepine	77
Quinidine hydrochloride monohydrate	59
Cyclobenzapine hydrochloride	77
Meclozine dihydrochloride	57
Efavirenz	101
Danuorubicin hydrochloride	87
Dosulepin hydrochloride	69
Metixene hydrochloride	95
Propafenone hydrochloride	79
Fluoxetine hydrochloride	65
Hexetidine	99
DO 897/99	90
Prenylamine lactate	93
Mometasone furoate	54
Dimethisoquin hydrochloride	101
Pinaverium bromide	74

	Promazine hydrochloride	75
	Chlorcyclizine hydrochloride	95
	Diphenylpryaline hydrochloride	69
	Proadifen hydrochloride	99
	Drofenine hydrochloride	98
	Cloperastine hydrochloride	100
	Methotrimeprazine maleate	87
	Trimipramine maleate	85
	Ethopropazine hydrochloride	67
	Trimeprazine tartrate	85
	Procyclidine hydrochloride	56
	Promethazine hydrochloride	67
	Fluspirilene	105
	S(-)Eticlopride hydrochloride	82
	Toremifene	94
	Canrenone	82
	Indtraline hydrochloride	104
	Naftopidil dihydrochloride	
	Pizotifen malate	104
	Zuclopenthixol dihydrochloride	99
	Alfaxalone	87
	Deptropine citrate	97
	Sertraline	67
	Halofantrine hydrochloride	111
	Penbutolol sulfate	69
	Piperacetazine	60
	Thiethylperazine dimalate	81
	Methiazole	79
	Toltrazuril	85
	Triclosan	71
	Aripiprazole	106
	Benztropine mesylate	93
	Ipriflavone	54
	Estramustine	57
	1,8-Dihydroxyanthraquinone	87
	Epirubicin hydrochloride	83
	Lomerizine hydrochloride	75

Supplemental table 5: Strains used in this study.

Strain	Genotype	Source
SC5314	*C. albicans* reference strain	(1)
CA1L-1	*C. albicans his1Δ/Δ arg4Δ/Δ cdr1Δ::HIS1/cdr1Δ::ARG4 ura3Δ/Δ:URA3*	(2)
MA3L-1	*C. albicans his1Δ/Δ arg4Δ/Δ mdr1Δ::HIS1/mdr1Δ::ARG4 ura3Δ/Δ:URA3*	(2)
ScMRR1M4A	*C. albicans mrr1Δ::FRT/mrr1Δ::FRT*	(3)
SZY33	*C. albicans tac1Δ::FRT/tac1Δ::*FRT *TAC1*	(4)
UPC2M4A	*C. albicans upc2-1Δ::FRT/upc2-2Δ::FRT*	(5)
UPC2R14A	*C. albicans UPC2*^{G648D}*-FRT/UPC2*^{G648D}*-FRT*	(6)
ScMRR1M4A	*C. albicans mrr1Δ::FRT/mrr1Δ::FRT*	(7)
ScTAC1R34A	*C. albicans TAC1*^{G980E}*-FRT/TAC1*^{G980E}*-FRT*	(8)
ATTC2001	*C. glabrata* reference strain	(9)
SM1	*C. glabrata* clinical isolate	(10)
SM1Δpdr1	*C. glabrata pdr1::FRT*	(11)
CDC 317	*C. parapsilosis* reference strain	(12)
MYA-3404	*C. tropicalis* reference strain	(13)
Ct 8	*C. tropicalis* clinical isolate 8	University of Iowa

Supplemental table 6: Oligonucleotides used in this study.

Primer	Sequence
ACT1- forward	ACG GTG AAG AAG TTG CTG CTT TAG TT
ACT1- reverse	CGT CGT CAC CGG CAA AA
CDR1- forward	ATT CTA AGA TGT CGT CGC AAG ATG
CDR1- reverse	AGT TCT GGC TAA ATT CTG AAT GTT TTC
CDR2- forward	TAG TCC ATT CAA CGG CAA CAT T
CDR2- reverse	CAC CCA GTA TTT GGC ATT GAA A
MDR1- forward	ACA TAA ATA CTT TGC CCA TCC AGA A
MDR1- reverse	AAG AGT TGG TTT GTA ATC GGC TAA A

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