

## Supplementary Information

### Point mutations in *Candida glabrata* 3-hydroxy-3-methyl glutaryl coenzyme A reductase (HMGRc) an antifungal target, decrease enzymatic activity and substrate/inhibitor affinity

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15	<i>Pseudomonas mevalonii</i>	-----MSLDS--RLPAFRNLSP-----AARLDHIGQLLGLSHDDVSLANAGALPM	44
16	<i>Arabidopsis thaliana</i>	DEEIVKSVIDG--VIPSYSLESRLGDCKRAASIRREALQRTGR---SIEGLPLDGFYDYE	55
17	<i>Drosophila melanogaster</i>	DEEIVSVHAGgtHCPLHKIESVLDDPERGVRIRRRQIIIGSRAKMPvgrLDVLPYEHFDYR	60
18	<i>Homo sapiens</i>	DAEIIQLVNAK--HIPAYKLETLMETHERGVSIRRQLLSKKLSEPs-sLQYLPYRDYNYS	57
19	<i>Mus musculus</i>	DAEIIQLVNAK--HIPAYKLETLMETHERGVSIRRQLLSTKLAEPs-sLQYLPYRDYNYS	57
20	<i>Rattus norvegicus</i>	DAEIIQLVNAK--HIPAYKLETLMETHERGVSIRRQLLSAKLAEPs-sLQYLPYRDYNYS	57
21	<i>Ustilago maydis</i>	DEEIIITLSQNG--KIAAYALEKVLQDHERAVVRRALVSRASATQtLeTSLPFRDYDYG	58
22	<i>Schizosaccharomyces pombe</i>	DEEVVQLTLAK--KIPLYALEKVLKDVTRAVVIRRTVVSRSSRTKtleSSNCFVYHYDYS	58
23	<i>Yarrowia lipolytica</i>	DHEVVKLSLEG--KLPLYALEKQLGDNTRAVGIRRSIIISQQSNTKtleTSKLPFAHYDYS	58
24	<i>Candida kefyr</i>	NREVSVLVVAN--KLPLYALEKQLGDTRAVVRRKALAILADAPvLaTERLPYKHYDYN	58
25	<i>Kluyveromyces lactis</i>	NKEVSVLVVNN--KLPLYALEKQLGDTRAVVRRKALAILADAPvLsTERLPYKHYDYS	58
26	<i>Candida glabrata</i>	NKEVSVLVIHG--KLPLYALEKQLGDTRAVCVRRKAI SILADAPvLaTDRLPYKHYDYS	58
27	<i>Saccharomyces HMG1</i>	NKEVAALVIHG--KLPLYALEKQLGDTRAVAVRRKALSILAEAPvLaSDRLPYKHYDYS	58
28	<i>Saccharomyces HMG2</i>	NTEVSNLVVNG--KLPLYSLEKKLEDTRAVLVRRKALSTLAESPILvSEKLPFRNYDYS	58
29	<i>Meyerozyma guilliermondii</i>	DNEVTNLVVSg--KLPLYALEKQLQDNTRAVVRRKAI AQMAGVpLdSDRLPYMHYDYN	58
30	<i>Clavispora lusitanae</i>	NSEVSVLVVAG--QLPLYALEKQLGNARAVVRRKAI AKLANAPvLeSNKLPFAHYDYS	58
31	<i>Candida auris</i>	NDEVSVLVVAG--KLPLYALEKQLGDNLRVAVVRRKAI AKLANAPvLdTKLPFAHYDYS	58
32	<i>Candida haemuloni</i>	NDEVSVLVVAG--KLPLYALEKQLQDNLRVAVVRRKAI AKLANAPvLdTERLPYAHYDYS	58
33	<i>Debaryomyces hansenii</i>	NNEISSLVVAG--KLPLYALEKQLADNTRAVLVRRKAI AKLANAPvLdTKLPYAHYDYS	58
34	<i>Candida parapsilosis</i>	NEEVTSLVVGG--KLPLYALEKQLASNKRAVVRRKAI AKLANAPvLeTNRLPYAHYDYS	58
35	<i>Candida orthopsilosis</i>	NEEVTSLVVGG--KLPLYALEKQLASNKRAVVRRKAI AKLANAPvLeTNRLPYAHYDYS	58
36	<i>Candida tropicalis</i>	NDEVSVLVVGG--KLPLYALEKQLGDNKRAVVRRKAI AKLANAPvLeSNRLPYSHYDYS	58
37	<i>Candida albicans</i>	NDEVSVLVVGG--KLPLYALEKQLADNKRAVVRRKAI AKLANAPvLdTNRLPYAHYDYS	58
38	<i>Candida dubliniensis</i>	NDEVSVLVVGG--KLPLYALEKQLADNKRAVVRRKAI AKLANAPvLdTNRLPYAHYDYS	58
39			

40	<i>Pseudomonas mevalonii</i>	DIANGMTEENVIGTFELPYAVASNFQINGRDVLPVPLVVEE	PSIVAASASYMAKLARANGGFT	104	
41	<i>Arabidopsis thaliana</i>	SILGQCCEMPVGYIQIPVGIAGPLLLLDGYEYSVPMATTE	EGCLVAS	TNRGCKAMFISGGAT	115
42	<i>Drosophila melanogaster</i>	KVLNACCENVLGYVPIPVGYAGPLLLDGETYYVPMATTE	EGALVAS	TNRGCKALSVRG-VR	119
43	<i>Homo sapiens</i>	LVMGACCENVIGYMPIPVGVAGPLCLDEKEFQVPMATTE	EGCLVAS	TNRGCRAIGLGGGAS	117
44	<i>Mus musculus</i>	LVMGACCENVIGYMPIPVGVAGPLCLDGKEYQVPMATTE	EGCLVAS	TNRGCRAISLGGGAS	117
45	<i>Rattus norvegicus</i>	LVMGACCENVIGYMPIPVGVAGPLCLDGKEYQVPMATTE	EGCLVAS	TNRGCRAISLGGGAS	117
46	<i>Ustilago maydis</i>	KVMGACCENVVGYMPLPLGIAGPLNIDGQFMPIPMATTE	EGTLVAS	TSRGCKALNAGGGVT	118
47	<i>Schizosaccharomyces pombe</i>	RVLNACCENVIGYMPLPVGVAGPLIIDGKPFYIPMATTE	EGALVAS	TMRGCKAINAGGGAV	118
48	<i>Yarrowia lipolytica</i>	RVFGACCENVIGYMPLPVGVAGPMNIDGKNYHIPMATTE	EGCLVAS	TMRGCKAINAGGGVT	118
49	<i>Candida kefyr</i>	RVFGACCENVIGYMPLPVGVIGPLMIDGVVYHIPMATTE	EGCLVAS	AMRGCKAINSGGGVT	118
50	<i>Kluyveromyces lactis</i>	RVFGACCENVIGYMPLPVGVIGPLMIDGVVYHIPMATTE	EGCLVAS	AMRGCCKAMNAGGGVQ	118
51	<i>Candida glabrata</i>	RVFGACCENVIGYMPLPVGVIGPLVIDGVSYPHIPMATTE	EGCLVAS	AMRGCCKAINAGGGVT	118
52	<i>Saccharomyces HMG1</i>	RVFGACCENVIGYMPLPVGVIGPLVIDGTSYHIPMATTE	EGCLVAS	AMRGCCKAINAGGGAT	118
53	<i>Saccharomyces HMG2</i>	RVFGACCENVIGYMPIPVGVIGPLIIDGTSYHIPMATTE	EGCLVAS	AMRGCCKAINAGGGAT	118
54	<i>Meyerozyma guilliermondii</i>	RVFGACCENVIGYMPIPVGVAGPLNIDGKSYHIPMATTE	EGCLVAS	TMRGCKAINAGGGVS	118
55	<i>Clavispora lusitaniae</i>	RVFGACCENVIGYMPLPVGVAGPLIIDGTPYHIPMATTE	EGCLVAS	AMRGCCKAINAGGGVE	118
56	<i>Candida auris</i>	RVFGACCENVIGYMPLPVGVAGPLIIDGVPHYIPMATTE	EGCLVAS	TMRGCKAINSGGGVQ	118
57	<i>Candida haemuloni</i>	RVFGACCENVIGYMPLPVGVAGPLIIDGTPYHVPMATTE	EGCLVAS	TMRGCKAINSGGGVQ	118
58	<i>Debaryomyces hansenii</i>	RVFGACCENVIGYMPLPVGVAGPLIIDGKPHYIPMATTE	EGCLVAS	TMRGCKAINAGGGVE	118
59	<i>Candida parapsilosis</i>	RVFGACCENVIGYMPIPVGVAGPLIIDGKPHYIPMATTE	EGCLVAS	AMRGCCKAINAGGGVE	118
60	<i>Candida orthopsilosis</i>	RVFGACCENVIGYMPIPVGVAGPLIIDGKPHYIPMATTE	EGCLVAS	TMRGCKAINAGGGVE	118
61	<i>Candida tropicalis</i>	RVFGACCENVIGYMPIPVGVAGPLVIDGKPHYIPMATTE	EGCLVAS	TMRGCKAINAGGGVE	118
62	<i>Candida albicans</i>	RVFGACCENVIGYMPLPVGVAGPLIIDKPHYIPMATTE	EGCLVAS	TMRGCKAINAGGGVE	118
63	<i>Candida dubliniensis</i>	RVFGACCENVIGYMPLPVGVAGPLIIDKPHYIPMATTE	EGCLVAS	TMRGCKAINAGGGVE	118
64					
65	<i>Pseudomonas mevalonii</i>	TSSSAPLMAHQVQIVGIQDPLNARLSLLRRKDEI---	IELANRKDQLLNSLGGGCRDIEV	161	
66	<i>Arabidopsis thaliana</i>	STVLKDKGMTRA-----P-VVRFASARRASELKFLENPENFDTLAVVFNRRSFRFAL		166	
67	<i>Drosophila melanogaster</i>	SVVEDVGMTRA-----P-CVRFPSVARAAEAKSWIENDENYRVVKTEFDSTSRFGRL		170	
68	<i>Homo sapiens</i>	SRVLADGMTRG-----P-VVRLPRACDSAEVKAWLETSEGFVAVKEAFDSTSRFARL		168	
69	<i>Mus musculus</i>	SRVLADGMTRG-----P-VVRLPRACDSAEVKTWLETPEGFVAVKEAFDSTSRFARL		168	
70	<i>Rattus norvegicus</i>	SRVLADGMSRG-----P-VVRLPRACDSAEVKSWLETPEGFVAVKEAFDSTSRFARL		168	
71	<i>Ustilago maydis</i>	TVLTDQDAMTRG-----P-ALEFPSSVVQAAKAKRWIDSQEQAQTIKAAFSTSRFARL		169	
72	<i>Schizosaccharomyces pombe</i>	TVLTRDQMSRG-----P-CVAFPNLTRAGRAKIWLDSPEGQEVMMKAFNSTSRFARL		169	
73	<i>Yarrowia lipolytica</i>	TVLTDQDGMTRG-----P-CVSFPKSLKRAGAAKIWLDSSEGLKSMRKAFNSTSRFARL		169	
74	<i>Candida kefyr</i>	TVLTKDGMTRG-----P-CVRFPSLKRAGACKIWLDSSEEGQNKIKKAFNSTSRFARL		169	
75	<i>Kluyveromyces lactis</i>	TVLTKDGMTRG-----P-CVRFPSLARAGACKIWLDSSEEGQNQIKKAFNSTSRFARL		169	
76	<i>Candida glabrata</i>	TVLTKDGMTRG-----P-CVRFPSLTRAGACKIWLDSSEEGQNQIKKAFNSTSRFARL		169	
77	<i>Saccharomyces HMG1</i>	TVLTKDGMTRG-----P-VVRFPTLKRSGACKIWLDSSEEGQNAIKKAFNSTSRFARL		169	
78	<i>Saccharomyces HMG2</i>	TVLTKDGMTRG-----P-VVRFPTLIRSGACKIWLDSSEEGQNSIKKAFNSTSRFARL		169	
79	<i>Meyerozyma guilliermondii</i>	TVLTDQDGMTRG-----P-CVSFPPLARAGAACKLWLDSSEEGQTIKKAFASTSRFARL		169	
80	<i>Clavispora lusitaniae</i>	TIITQDGMTRG-----P-CVSFSSLARAGACKLWLDSSEEGQTIKKAFASTSRFARL		169	
81	<i>Candida auris</i>	TILTQDGMTRG-----P-CVSFPSSLARAGACKLWLDSSEEGQRTIKKAFNSTSRFARL		169	
82	<i>Candida haemuloni</i>	TILTQDGMTRG-----P-CVSFPSSLARAGACKLWLDSSEEGQRTIKKAFNSTSRFARL		169	
83	<i>Debaryomyces hansenii</i>	SVLTQDGMTRG-----P-CVSFPSSLRAGACKLWLDSSEEGQTIKKAFASTSRFARL		169	
84	<i>Candida parapsilosis</i>	TVLTKDGMTRG-----P-CVRFPTLSRAGAACKLWLDSSEEGQTIKKAFASTSRFARL		169	
85	<i>Candida orthopsilosis</i>	TVLTKDGMTRG-----P-CVKFPTLARAGAACKLWLDSSEEGQTIKKAFASTSRFARL		169	
86	<i>Candida tropicalis</i>	TVLTKDGMTRG-----P-CVRFPTLKRAGAACKLWLDSSEEGQTIKKAFASTSRFARL		169	
87	<i>Candida albicans</i>	TVLTRDGMTRG-----P-CVRFPTLKRAGAACKLWLDSSEEGQATIKKAFASTSRFARL		169	
88	<i>Candida dubliniensis</i>	TVLTRDGMTRG-----P-CVRFPTLKRAGAACKLWLDSSEEGQATIKKAFASTSRFARL		169	
89					
90	<i>Pseudomonas mevalonii</i>	HTFADTFRGPMLVAHLIVDVR	DAMGMAN	TVNTMAEAVAPLMEAITGGQVRLRILSNLADLR	221
91	<i>Arabidopsis thaliana</i>	QSVKCTIAGKNAYVRFCCSTG	DAMGMNMVSKGVQNVLEYLTD	---FPDMDVIGISGNFC	223
92	<i>Drosophila melanogaster</i>	KDCHIAMDGPQLYIRFVAITG	DAMGMNMVSKGAEMALRRIQL	--Q-FPDMQIISLSGNFC	227
93	<i>Homo sapiens</i>	QKLHTSIAGRNLIRFQSRSG	DAMGMNMISKGTEKALS	KLHEY---FPQMILAVSGNYC	225
94	<i>Mus musculus</i>	QKLHVTMAGRNLIRFQSRSG	DAMGMNMISKGTEKALLKLQEF	---FPDMQILAVSGNYC	225
95	<i>Rattus norvegicus</i>	QKLHVTLAGRNLIRLQSKTG	DAMGMNMISKGTEKALLKLQEF	---FPQLAVSGNYC	225
96	<i>Ustilago maydis</i>	SSLRCVLAGRNLIRVFATSTG	DAMGMNMISKGVEKALGLMTEQY	--FpEMKVLVSLSGNYC	227
97	<i>Schizosaccharomyces pombe</i>	QHIKTALAGTRLIRFCTSTG	DAMGMNMISKGVEHALVMSNDAG	-fdDMQVIVSVSGNYC	228
98	<i>Yarrowia lipolytica</i>	QSLHSTLAGNLLIRFRTTTG	DAMGMNMISKGVEHSLAVMVEEY	-fpDMDIVSVSGNYC	228
99	<i>Candida kefyr</i>	QHVQALAGDLLIRFRTTTG	DAMGMNMISKGVEFSLHQMVVEEY	-wkDMEIVSVSGNYC	228
100	<i>Kluyveromyces lactis</i>	QHIQTALAGDLLIRFRTTTG	DAMGMNMISKGVEFSLKQMVVEEY	-wnDMEIVSVSGNYC	228
101	<i>Candida glabrata</i>	QHAQTALAGDLLIRFRTTTG	DAMGMNMISKGVEFVLKQMVVEEY	-whDMEIVSVSGNYC	228
102	<i>Saccharomyces HMG1</i>	QHIQTCLAGDLLFMRFTTTG	DAMGMNMISKGVEYSLKQMVVEEY	-weDMEVSVSGNYC	228
103	<i>Saccharomyces HMG2</i>	QHIQTCLAGDLLFMRFTTTG	DAMGMNMISKGVEYSLKQMVVEEY	-weDMEVSVSGNYC	228
104	<i>Meyerozyma guilliermondii</i>	QHIKTALAGTLLIRFRTTTG	DAMGMNMISKGVEYCLKHMVEEY	-fkDMTVIVSVSGNYC	228
105	<i>Clavispora lusitaniae</i>	QHIKTAIAGTLLIRFRTTTG	DAMGMNMISKGVEYSLKYMAEEY	-wdDMSVIVSVSGNYC	228
106	<i>Candida auris</i>	QHVKTAIAGTLLIRFRTTTG	DAMGMNMISKGVEHSLKFMVEEY	-feDMSVIVSVSGNYC	228
107	<i>Candida haemuloni</i>	QHVKTAIAGTLLIRFRTTTG	DAMGMNMISKGVEHSLKFMVEEY	-fdDMSVIVSVSGNYC	228

108	<i>Debaryomyces hansenii</i>	QHIQTALAGTLLFIRFRRTTGGDAMGMNMISKGVEYSLKYMSEECD-wsDMEVIVSVSGNYC	228
109	<i>Candida parapsilosis</i>	QHIQTSLAGCLLFIRFRRTTGGDAMGMNMISKGVEYSLKYMVEECG-yeDMEIISVSGNYC	228
110	<i>Candida orthopsilosis</i>	QHIQTALAGCLLFIRFRRTTGGDAMGMNMISKGVEHSLKYMVEECG-yeDMEIISVSGNYC	228
111	<i>Candida tropicalis</i>	QHIQTALAGTSLFVFRRTTGGDAMGMNMISKGVEYSLKYMVEECG-wdDMEVIVSVSGNYC	228
112	<i>Candida albicans</i>	QHIQTALAGTSLFIRFRRTTGGDAMGMNMISKGVEYSLKYMVEECG-wdDMEIVSVSGNYC	228
113	<i>Candida dubliniensis</i>	QHIQTALAGTSLFIRFRRTTGGDAMGMNMISKGVEYSLKYMVEECG-wdDMEIVSVSGNYC	228
114			
115	<i>Pseudomonas mevalonii</i>	LARAQVRI TPQOLETAEFSGE-----AVIEG-----ILDAYAFAAVDPYR----A-----	262
116	<i>Arabidopsis thaliana</i>	SD-----KKPAAVNWIEGRGKSVVCEAVIRGEIVNKLKTSVAALVELNMLKNLAGSAVA	278
117	<i>Drosophila melanogaster</i>	CD-----KKPAAINWIKGRGKRVVTECTISAATLRSVLKTDKATLVECNKLNKMGGSAMA	282
118	<i>Homo sapiens</i>	TD-----KKPAAINWIEGRGKSVVCEAVIPAKVVREVLKTTTEAMIEVNNINKNLVGSAMA	280
119	<i>Mus musculus</i>	TD-----KKPAAINWIEGRGKSVVCEAVIPAKVVREVLKTTTEAMVDVNNINKNLVGSAMA	280
120	<i>Rattus norvegicus</i>	TD-----KKPAAINWIEGRGKTVVCEAVIPAKVVREVLKTTTEAMVDVNNINKNLVGSAMA	280
121	<i>Ustilago maydis</i>	TD-----KKPAAINWIEGRGKSVVAEAVVPGNVVRSVLKCTVRDLVNLNTKKNLIGSAMA	282
122	<i>Schizosaccharomyces pombe</i>	TD-----KKPAAINWIDGRGKSVIAEAIIPGDVAVKSVLKTTEVDLVLKLVNVDKNLIGSAMA	283
123	<i>Yarrowia lipolytica</i>	TD-----KKPAAINWIEGRGKSVVAEATIPAHIVKSVLKSEVDALVELNISKNLIGSAMA	283
124	<i>Candida kefyr</i>	MD-----KKPAAINWIEGRGKSVVAEANIIPGDVVRKVLKSDVKALVDLNLISKNLIGSAMA	283
125	<i>Kluyveromyces lactis</i>	MD-----KKPAAINWIEGRGKSVVAEATIPGDVVRKVLKSDVKALVDLNLISKNLIGSAMA	283
126	<i>Candida glabrata</i>	TD-----KKPAAINWIEGRGKSVIAEAIIPGDVVRKVLKSDVSALVELNISKNLIGSAMA	283
127	<i>Saccharomyces HMG1</i>	TD-----KKPAAINWIEGRGKSVVAEATIPGDVVRKVLKSDVSALVELNISKNLIGSAMA	283
128	<i>Saccharomyces HMG2</i>	TD-----KKPAAINWIEGRGKSVVAEATIPGDVVKSVLKSDVSALVELNISKNLVGSAMA	283
129	<i>Meyerozyma guilliermondii</i>	TD-----KKPSAINWIEGRGKSVVAEARIIPADVKNVVKLSDVDALVELNVSKNLVGSAMA	283
130	<i>Clavispora lusitanae</i>	TD-----KKPAAINWIEGRGKSVVAEARIIPSEVVQKVLKSDVDALVELNISKNLIGSAMA	283
131	<i>Candida auris</i>	TD-----KKPAAINWIEGRGKSVVAEARIIPADVVRKVLKSDVDALVELNISKNLVGSAMA	283
132	<i>Candida haemuloni</i>	TD-----KKPAAINWIEGRGKSVVAEARIIPKDVVEKVLKSDVDALVELNVSKNLVGSAMA	283
133	<i>Debaryomyces hansenii</i>	TD-----KKPAAINWIEGRGKSVVAEARIIPASVVQKVLKSDVDALVELNISKNLVGSAMA	283
134	<i>Candida parapsilosis</i>	SD-----KKPAAINWIEGRGKSVIAEATIPADVAVKVLKSDVDALVELNISKNLVGSAMA	283
135	<i>Candida orthopsilosis</i>	SD-----KKPAAINWIEGRGKSVIAEATIPADVAVKVLKSDVDALVELNISKNLVGSAMA	283
136	<i>Candida tropicalis</i>	TD-----KKPAAINWIEGRGKSVIAAATIPAEVVTKVLKSDVDALVELNISKNLVGSAMA	283
137	<i>Candida albicans</i>	TD-----KKPAAINWIEGRGKSVIAAARIIPADVVTKVLKSDVDALVELNISKNLVGSAMA	283
138	<i>Candida dubliniensis</i>	TD-----KKPAAINWIEGRGKSVIAAARIIPADVVTKVLKSDVDALVELNISKNLVGSAMA	283
139			
140	<i>Pseudomonas mevalonii</i>	---ATHNKGIMNGIDPLIVATGNDWRAVEAGAHAYACRSGHYGLTTEWEDKDNHGLVGTG	319
141	<i>Arabidopsis thaliana</i>	GSLGGFNAAHASNIVSAVFIATGQDPAQ-----NVESSQCITMMEAIND-GKDIHISV	329
142	<i>Drosophila melanogaster</i>	GSIGGNNAHAANMVTAVFLATGQDPAQ-----NVTSSNCSTAMECWAENSEDLYMT	334
143	<i>Homo sapiens</i>	GSIGGYNAHAANIVTAIYIACGQDAAQ-----NVGSSNCITLMEASGpTNEDLYISC	332
144	<i>Mus musculus</i>	GSIGGYNAHAANIVTAIYIACGQDAAQ-----NVGSSNCITLMEASGpTNEDLYISC	332
145	<i>Rattus norvegicus</i>	GSIGGYNAHAANIVTAIYIACGQDAAQ-----NVGSSNCITLMEASGpTNEDLYISC	332
146	<i>Ustilago maydis</i>	GSVGGFNAAHANILTAIYLATGQDPAQ-----NVESSNCITLMEAIND-DEDLLITV	333
147	<i>Schizosaccharomyces pombe</i>	GSVGGFNAAHANIVTAIYLATGQDPAQ-----NVESSNCITLMDNV---DGNLLISV	332
148	<i>Yarrowia lipolytica</i>	GSVGGFNAAHANLVTAIYLATGQDPAQ-----NVESSNCITLMSNV---DGNLLISV	332
149	<i>Candida kefyr</i>	GSIGGFNAHASNLVTAIVYLLALGQDPAQ-----NVESSNCITLMKEV---DGDRLISV	332
150	<i>Kluyveromyces lactis</i>	GSVGGFNAAHASNLVSAVFLALGQDPAQ-----NVESSNCITLMKEV---DGDRLISV	332
151	<i>Candida glabrata</i>	GSVGGFNAAHANLVTAVYLLALGQDPAQ-----NVESSNCITLMDNV---NGDLKISV	332
152	<i>Saccharomyces HMG1</i>	GSVGGFNAAHANLVTAVYLLALGQDPAQ-----NVESSNCITLMKEV---DGDRLISV	332
153	<i>Saccharomyces HMG2</i>	GSVGGFNAAHANLVTALFLALGQDPAQ-----NVESSNCITLMKEV---DGDRLISV	332
154	<i>Meyerozyma guilliermondii</i>	GSVGGFNAAQANLVTAVFLACGQDPAQ-----NVESSNCITLVNKV---DGDLLISV	332
155	<i>Clavispora lusitanae</i>	GSVGGFNAAHANLVTAVYLLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	332
156	<i>Candida auris</i>	GSVGGFNAAHANLVTAVYLLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	332
157	<i>Candida haemuloni</i>	GSVGGFNAAHANLVTAVFLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	332
158	<i>Debaryomyces hansenii</i>	GSVGGFNAAHANLVTAVFLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	332
159	<i>Candida parapsilosis</i>	GSVGGFNAAHASNLVTAIVYLLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	334
160	<i>Candida orthopsilosis</i>	GSVGGFNAAHASNLVTAIVYLLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	334
161	<i>Candida tropicalis</i>	GSVGGFNAAHANLVTAVYLLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	334
162	<i>Candida albicans</i>	GSVGGFNAAHANLVTAVYLLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	334
163	<i>Candida dubliniensis</i>	GSVGGFNAAHANLVTAVYLLACGQDPAQ-----NVESSNCITLMDNV---DGDLLISV	334
164			
165	<i>Pseudomonas mevalonii</i>	EMP-MPVGLVGGATKTHPLAQLSLRILGVKTA-----QALAEIAVAVGLAQNLGAM	369
166	<i>Arabidopsis thaliana</i>	TMPSIEVGTVGGGTQLASQS-ACLNLLGVKGASTESPGMNARRLATIVAGAVLAGELSLM	388
167	<i>Drosophila melanogaster</i>	TMPSLEVGTVGGGTGLPGQS-ACLEMLGVRGAHATRPDGNKLAQIVCATVMAGELSLM	393
168	<i>Homo sapiens</i>	TMPSIEIGTVGGGTNLLPQQ-ACLQMLGVQGACKDNPGENARQLARIVCGTVMAGELSLM	391
169	<i>Mus musculus</i>	TMPSIEIGTVGGGTNLLPQQ-ACLQMLGVQGACKDNPGENARQLARIVCGTVMAGELSLM	391
170	<i>Rattus norvegicus</i>	TMPSIEIGTVGGGTNLLPQQ-ACLQMLGVQGACKDNPGENARQLARIVCGTVMAGELSLM	391
171	<i>Ustilago maydis</i>	SMPSIEVGTVGGGTVLPQQR-SMLEMMGIAGAHSTTPGANAQRLARI IAASVMAGELSLM	392
172	<i>Schizosaccharomyces pombe</i>	SMPSIEVGTIGGGTILEPQG-AMLDDLGVVRGAMHTSPGDNSRQLARIVAAVMAGELSLC	391
173	<i>Yarrowia lipolytica</i>	SMPSIEVGTIGGGTILEPQG-AMLEMLGVRGPHIETPGANAQQLARI IASVGLAAELSLC	391
174	<i>Candida kefyr</i>	SMPSIEVGTIGGGTILEPQS-AMLDDLGVVRGPHPTPEPGKNAQQLAKIVASAVMAGELSLC	391
175	<i>Kluyveromyces lactis</i>	SMPSIEVGTIGGGTILEPQG-AMLDDLGVVRGPHPTQPNNARQLAKIVASAVMAGELSLC	391

176	<i>Candida glabrata</i>	SMPSIEVGTIGGGTVLDFPQG-AMLDLLGVGRPHPTNPGANARQLAKIVACAVLAGELSLC	391
177	<i>Saccharomyces HMG1</i>	SMPSIEVGTIGGGTVLEFPQG-AMLDLLGVGRPHATAPGTNARQLARIVACAVLAGELSLC	391
178	<i>Saccharomyces HMG2</i>	SMPSIEVGTIGGGTVLEFPQG-AMLDLLGVGRPHPTNPGANARQLARIACAVLAGELSLC	391
179	<i>Meyerozyma guilliermondii</i>	SMPSIEVGTIGGGTILEFPQG-AMLDLLRVKGPHTNPGENARQLARIVASAVLAAELSLC	391
180	<i>Clavispora lusitaniae</i>	SMPSIEVGTIGGGTILEFPQG-AMLELLGVGRPHPTNPGDNRRLACIVASAVLAAELSLC	392
181	<i>Candida auris</i>	SMPSIEVGTIGGGTILEAQG-SMLDLLGVGRPHPKNPGDNRRLACIVASAVLAAELSLC	391
182	<i>Candida haemuloni</i>	SMPSIEVGTIGGGTILEAQG-SMLDLLGVGRPHNNPGDNRRLACIVASTVLAELSLC	391
183	<i>Debaryomyces hansenii</i>	SMPCIEVGTIGGGTILEFPQG-AMLDLLGVGRPHPTNPGDNRQLARIVASAVLAAELSLC	391
184	<i>Candida parapsilosis</i>	SMPSIEVGTIGGGTILEFPQG-AMLDLLGVGRPHPTNPGDNRQLAKIVASAVLAAELSLC	393
185	<i>Candida orthopsilosis</i>	SMPSIEVGTIGGGTILEFPQG-AMLDLLGVGRPHPTNPGDNRQLAKIVASAVLAAELSLC	393
186	<i>Candida tropicalis</i>	SMPSIEVGTIGGGTILEFPQG-AMLELLGVGRPHPTNPGDNRQLAKIVASAVLAAELSLC	393
187	<i>Candida albicans</i>	SMPSIEVGTIGGGTILEFPQG-AMLDLLGVGRPHPTNPGANAQQLAKIVASAVLAAELSLC	393
188	<i>Candida dubliniensis</i>	SMPSIEVGTIGGGTILEFPQG-AMLDLLGVGRPHPTNPGENARQLAKIVASAVLAAELSLC	393
189			
190	<i>Pseudomonas mevalonii</i>	RALATEGIQRGHMALHARNIAVVAGARGDEVWVARQLVEYHDVVRADRAVALLKQKRGQ	428
191	<i>Arabidopsis thaliana</i>	SATAAGQLVRSHEMKNRS-----	406
192	<i>Drosophila melanogaster</i>	AALVNSDLVKSHMRHNR-----	410
193	<i>Homo sapiens</i>	AALAAGHLVKSHMIHNR-----	409
194	<i>Mus musculus</i>	AALAAGHLVRSHEMKNRS-----	409
195	<i>Rattus norvegicus</i>	AALAAGHLVRSHEMKNRS-----	409
196	<i>Ustilago maydis</i>	GALCAGHLIQAHMKHNR-----	410
197	<i>Schizosaccharomyces pombe</i>	SALASGHLVKSHIIGLNR-----	409
198	<i>Yarrowia lipolytica</i>	SALAAGHLVQSHMTHNR-----	408
199	<i>Candida kefyr</i>	SALAAGHLVQSHMKNRS-----	408
200	<i>Kluyveromyces lactis</i>	SALAAGHLVQSHMKNRS-----	408
201	<i>Candida glabrata</i>	AALAAGHLVQSHMTHNR-----	408
202	<i>Saccharomyces HMG1</i>	AALAAGHLVQSHMTHNR-----	408
203	<i>Saccharomyces HMG2</i>	SALAAGHLVQSHMTHNR-----	408
204	<i>Meyerozyma guilliermondii</i>	SALAAGHLVQSHMQHNR-----	408
205	<i>Clavispora lusitaniae</i>	SALAAGHLVQSHMQHNR-----	409
206	<i>Candida auris</i>	SALAAGHLVQSHMQHNR-----	408
207	<i>Candida haemuloni</i>	SALAAGHLVQSHMQHNR-----	408
208	<i>Debaryomyces hansenii</i>	SALAAGHLVQSHMQHNR-----	408
209	<i>Candida parapsilosis</i>	SALAAGHLVQSHMQHNR-----	410
210	<i>Candida orthopsilosis</i>	SALAAGHLVQSHMQHNR-----	410
211	<i>Candida tropicalis</i>	SALAAGHLVQSHMQHNR-----	410
212	<i>Candida albicans</i>	SALAAGHLVQSHMQHNR-----	411
213	<i>Candida dubliniensis</i>	SALAAGHLVQSHMQHNR-----	410
214			

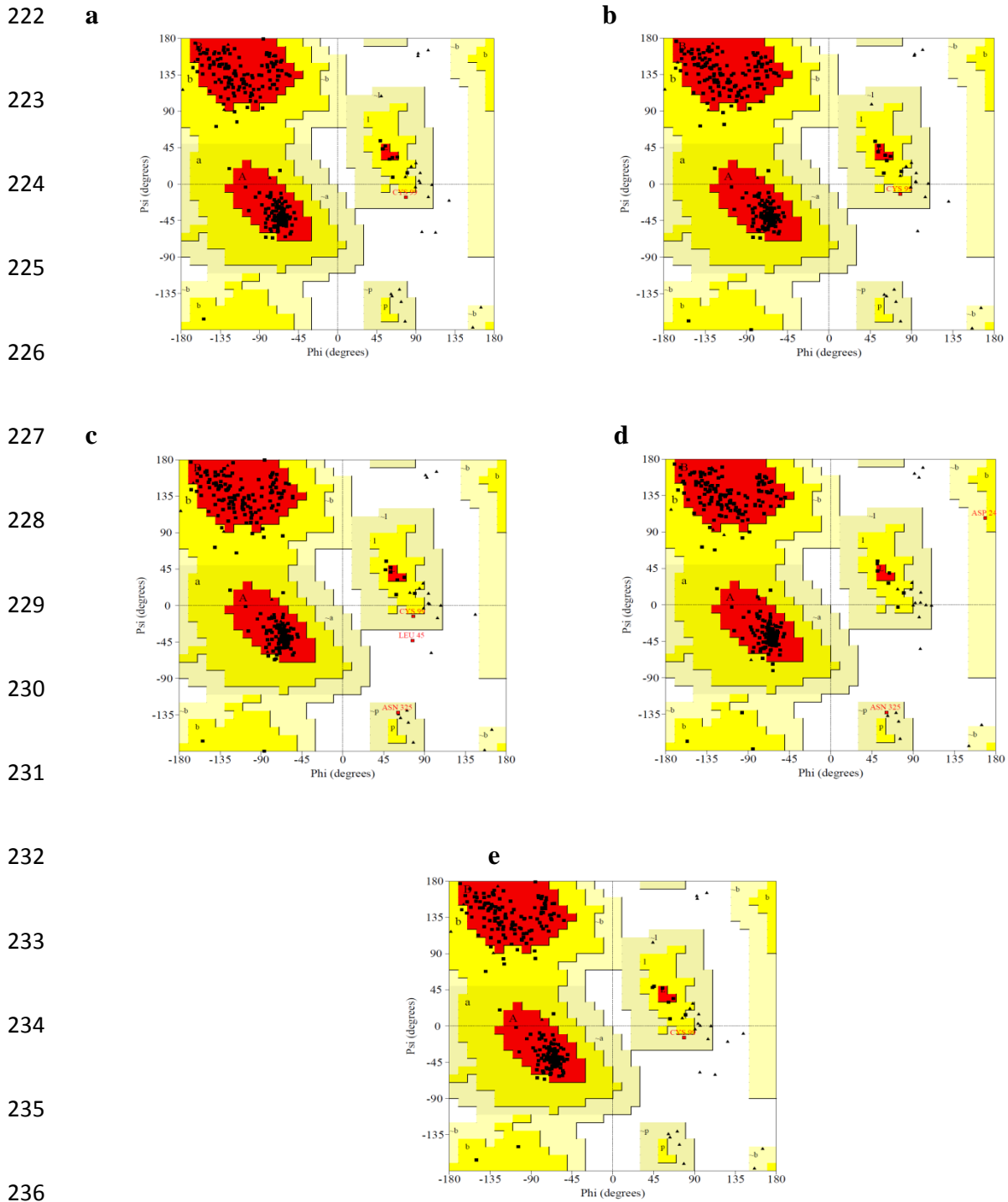
215 **Supplementary Figure S1.** Multiple sequence alignment of the catalytic portions of the HMGRs  
216 from different organisms. The dimerization domain is highlighted in yellow, the substrate binding  
217 domain in green and the cofactor binding domain cyan.

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237 **Supplementary Figure S2.** Ramachandran plots of the mutated HMGR proteins of *Candida*  
 238 *glabrata* (HMGRc): (a) HMGRcE680Q, (b) HMGRcE711Q, (c) HMGRcD805A, (d)

239 HMGRcM807R and (e) HMGRc E680Q-M807R. The residues are portrayed with black  
240 squares, being A, B, and L in the favored region (red zones), a, b, l, and p in the allowed region  
241 (yellow zones), and ~ a, ~ b, ~ l, and ~ p in the generously allowed region (beige zones). No  
242 residues were found in the disallowed region (white zones).

243

**a****b**

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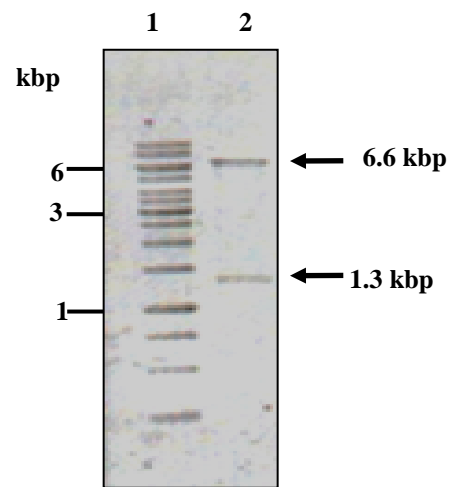
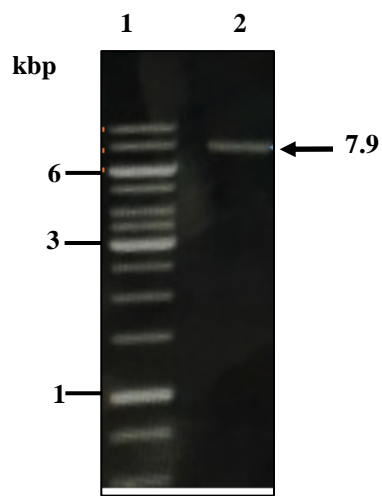
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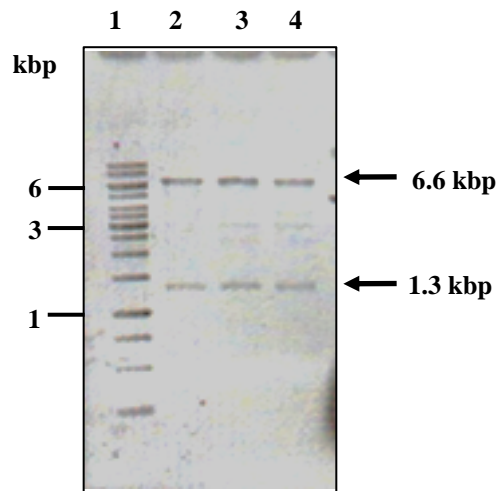
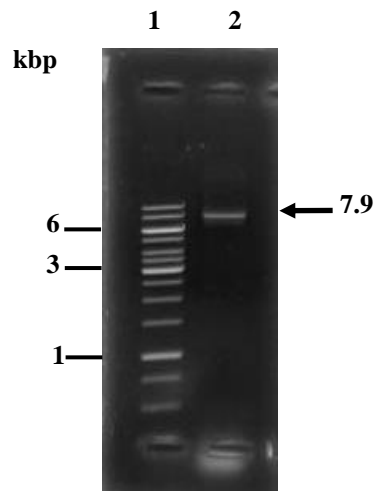
**c****d**

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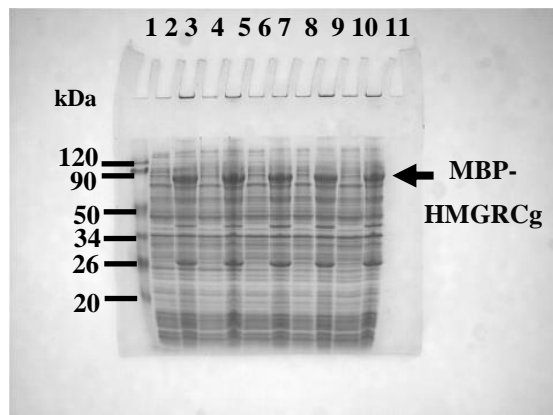
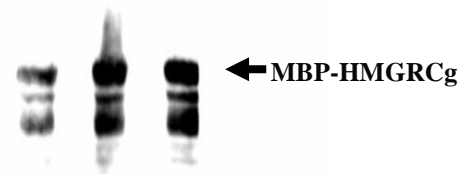
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255



256 **Supplementary Figure S3.** Through amplification and digestion, the HMGRc mutants  
 257 obtained by mutagenic PCR were verified. **(a)** Amplification of the HMGRc mutant: Lane 1, the  
 258 1 kbp molecular size marker; lane 2, the 7.9 kbp product. **(b)** Digestion of the plasmids of the  
 259 HMGRc mutants by the BamHI and Sall enzymes: Lane 1, the 1 kbp marker; lane 2, the products  
 260 of double digestion: 6.6 and 1.3 kbp. **(c)** Full-length gel original-amplification PCR,  
 261 corresponding to Fig. S2a. **(d)** Full-length gel original-digestion plasmid, corresponding Fig.S2b.

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263 **a**263 **b**

270 **Supplementary Figure S4.** Full-length gel/blots are displayed. **(a)** Full-length original gel  
 271 corresponding to Fig. 6b in main text. **(b)** Full-length blots original, corresponding Fig.6c in main  
 272 text.

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276 **Supplementary Table S1. Statistics for the Ramachandran plots constructed for the protein**  
 277 **models of mutated HMGR of *Candida glabrata* (HMGRcG).**

Ramachandran plot statistics	HMGRcGE68 0Q		HMGRcGE71 1Q		HMGRcGD80 5A		HMGRcGM80 7R		HMGRcGE76 80Q-M807R	
	Residues	%	Residues	%	Residues	%	Residues	%	Residues	%
Most favored regions	331	95.1	329	94.5	324	93.1	326	93.7	327	94
Allowed regions	16	4.6	18	5.2	21	6	20	5.7	20	5.7
Generously allowed regions	1	0.3	1	0.3	2	0.6	2	0.6	1	0.3
Disallowed regions	0	0	0	0	1	0.3	0	0	0	0
Non-glycine and non-proline residues	348	100	348	100	348	100	348	100	348	100
End residues (excluding Gly and Pro)	2	—	2	—	2	—	2	—	2	—
Glycine residues	41	—	41	—	41	—	41	—	41	—
Proline residues	17	—	17	—	17	—	17	—	17	—

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