

Supplementary Information

Unique structural features in a deep-sea CYP51 relate to high pressure adaptation

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C. armatus : ~~~~~~AKKTKC :
Human : MLLGLLQAGGSILGQAMEKVTGGNLSMLLIACAFITSLIVYLIIRLAAGHLVQ-LPAGVKS : 60
KAJ3609750 : ~~~MAAAPWYQTMFGEAMGRLLSSDGLTSAVLAASVIALALGFLSKRLIQC-AS-SSTDIKY : 56
XP_030203989 : ~~~MAAPLYQMLFGDTVGM-SDNLTSVFLAVSVITIALGYLSKMMIQC-ST-SDPNVKY : 54
XP_0564381 : ~~~MAAPLYQMLFGDTVGM-SDNLTSVFLAVSVITIALGYLSKMMIQC-ST-SDPNVKY : 54
KAK0136477 : ~~~MAAPSYQTMFADAVGKVVSDHLTSVLLAASLVITIALGYLSKVLLQC-T---PPDIKY : 53
NP_001001730 : ~~~MTILEVGSQIESAV--L-QMSLTSVLLTASVFTITLGYFSKLIFTCHS---SEHTKY : 52
XP_029591193 : ~MAMHLYQVSSMLLENTVGM-SDNLTSVVLAASVITITLGYISKLVIKSQSSSEEHKKY : 59
XP_036948155 : ~MSLHLYEMSSKIFGETVGM-NENLTSVVLAASLVITIIIGYVSKVLLKCSS--DSEDKKY : 57
XP_010739985 : ~~~MHFYEMSSRLIGDTVSKV-TDNVTTVVLAASVITITLGYVSKVLLRCSS--D-KDIKY : 54
KAF3707363 : ~~~MQLYQLSSKILGDTVGM-NDNLTISVLAASALTITLGYISKLLRCSS--D-KDIKC : 54
QQL94751_1 : ~MSVLIFYELSSRLVDAVGKM-NDNLTSVVLAASVITITLGYVSNVLLRCPP--D-ADIKY : 56
XP_039976906 : ~MSMHFYQISSKILGDTVGM-NDNLTISVLAASVITITLGYISKMLRCSS--D-KDIKY : 56
XP_034066366 : ~MSVQFYEMGSRIFGDTVGM-SDNLTSVVLAASVITIALGYITKMLLKESP--D-TDIKY : 56
XP_033950401 : ~MSVQFYEMGSRIFGDTVGM-SDNLTSVVLAASVITIALGYITKMLLKESP--D-TDIKY : 56
XP_037650187 : ~MAHLYEMSSKILGDTVGM-SDNLTSVVLAASVITITLGYLSKMLLKCSS--D-SDIKY : 56
XP_031722207 : ~MSFHYEMSSKILGDTVGMT-NDNLTSVVLAASVITITLGYLSKLLKPSS--D-NDIKY : 56

C. armatus : PPVIFSRIPFLGHAVAFGKNPIEFLEKAYEKYGVVSFTMVGKTFTFLLGSDAAALMFNSK :
Human : PPVIFSPIPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGKTFTTYLLGSDAAALLFNSK : 121
KAJ3609750 : PPVIFSRIPFLGHAVAFGKSPIEFLENAYEKYGVVSFTMVGKTFTFLLGSDAAALMFNSK : 117
XP_030203989 : PPVIFSRIPFLGHAVAFGKSPIEFLEKAYEKYGVVSFTMVGKTFTFLLGSDAASLMFNSK : 115
XP_0564381 : PPVIFSRIPFLGHAVAFGKSPIEFLEKAYEKYGVVSFTMVGKTFTFLLGSDAASLMFNSK : 115
KAK0136477 : PPVIFSRIPFLGHAVAFGKSPIEFLEKAYEKYGVVSFTMVGKTFTFLLGSDAAALMFNSK : 114
NP_001001730 : PPVIFSSLPFLGHAVAFGRSPIEFLEKAYEQYGVVSFTMVGKTFTTYLLGSDAAALMFNSK : 113
XP_029591193 : PPVIFSSIPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGKTFTTYLLGSEAAATLMFNSK : 120
XP_036948155 : PPVIFSSIPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGSTFTTYLLGSEAAATLMFNSK : 118
XP_010739985 : PPVIFSSIPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGSTFTTYLLGSDAAQLMFNSK : 115
KAF3707363 : PPVIFSSIPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGKTFTTYLLGSEAAALMFNSK : 115
QQL94751_1 : PPVIFSSVPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGSTFTTYLLGSDAATLMFNSK : 117
XP_039976906 : PPVIFSSVPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGKTFTTYLLGSEAAATLMFNSK : 117
XP_034066366 : PPVIFSSIPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGSTFTTYLLGSEAAATLMFNSK : 117
XP_033950401 : PPVIFSSIPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGSTFTTYLLGSEAAATLMFNSK : 117
XP_037650187 : PPVIFSSIPFLGHAFAGKSPIEFLENAYEKYGVVSFTMVGSTFTTYLLGSEAAATLMFNSK : 117
XP_031722207 : PPVIFSSIPFLGHAFAGRSPIEFLEHAYEKYGVVSFTMVGSTFTTYLLGSEAAATLMFNSK : 117

C. armatus : NEDLSAEDVYSKITTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAQFKKHVPIIEQETEEY :
Human : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKSGLNIAHFQKHVSIIIEKETKEY : 182
KAJ3609750 : NEDLSAEDVYSKITTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAQFKKHVTIIENETEEY : 178
XP_030203989 : NEDLSAEDVYSKITTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAQFKKHVSLIEDETVEY : 176
XP_0564381 : NEDLSAEDVYSKITTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAQFKKHVSLIEDETVEY : 176
KAK0136477 : NEDLSAEDVYSKITTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAQFKKHVAIIIEKETQY : 175
NP_001001730 : NEDLNAEDVYARLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAQFKQHVIIIEETKDY : 174
XP_029591193 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAHFQKHVEIIIEETKEY : 181
XP_036948155 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAHFREHVKVIEAETIEY : 179
XP_010739985 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAHFREHVKIIIEAETKEY : 176
KAF3707363 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKSGLNIAHFKEHVKIIIEAETIDY : 176
QQL94751_1 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAHFQKHVKVIEAETIEY : 178
XP_039976906 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAHFKEHVKIIIEAETVEY : 178
XP_034066366 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAHFKEHVKIIIEAETIEY : 178
XP_033950401 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFMEQKKMLKTGLNIAHFKEHVKIIIEAETIEY : 178
XP_037650187 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAHFKEHMKIIIEAETIEY : 178
XP_031722207 : NEDLNAEDVYSRLTTPVFGKGVAYDVPNPIFLEQKKMLKTGLNIAHFKEHVKIIIEAETIKY : 178

C. armatus : IKRWGDSGETNLFVAMSELIILTASSCLHGKEIRSMLEKVAQLYCDLDGGFSHEAWLLPS :
Human : FESWGDSGEKNLFVASELIILTASSCLHGKEIRSMLEKVAQLYADLDGGFSHAAWLLPG : 243
KAJ3609750 : MKRWGDSGETNLFVASELIILTASSCLHGKEIRSMLEKVAQLYCDLDGGFSHEAWLLPS : 239
XP_030203989 : MKRWGDSGETNLFVASELIILTASSCLHGKEIRSMLEKVAQLYCDLDGGFSHEAWLLPS : 237
XP_0564381 : MKRWGDSGETNLFVASELIILTASSCLHGKEIRSMLEKVAQLYCDLDGGFSHEAWLLPS : 237
KAK0136477 : IKRWGDSGETNLFVASELIILTASSCLHGKEIRSMLEKVAQLYDLDGGFSHEAWLLPS : 236
NP_001001730 : FERWGDSGERNLFVASELIILTASSCLHGCEIRSMLEKVAQLYADLDGGFTHAAWLLPG : 235
XP_029591193 : FSRWGDSGEQNLFVASELIILTASSCLHGKEIRSMLEKVAQLYADLDGGFSHAAWLLPG : 242
XP_036948155 : FORWGDSGEKNLFVASELIILTASSCLHGKEIRSMLEKVAQLYADLDGGFSHAAWLLPG : 240
XP_010739985 : FORWGDSGERNLFVASELIILTASSCLHGKEIRSMLEKVAQLYADLDGGFSHAAWLLPG : 237
KAF3707363 : FORWGDSGERNLFVASELIILTASSCLHGKEIRSMLEKVAQLYADLDGGFTHAAWLLPG : 237
QQL94751_1 : FERWGDSGEKNLFVASELIILTASSCLHGKEIRSMLEKVAQLYADLDGGFSHAAWLLPG : 239
XP_039976906 : FORWGDSGERNLFVASELIILTASSCLHGKEIRSMLEKVAQLYADLDGGFSHAAWLLPG : 239
XP_034066366 : FORWGDSGEKNLFVASELIILTASSCLHGKEIRSMNEHVAQLYADLDGGFSHAAWLLPG : 239
XP_033950401 : FORWGDSGEKNLFVASELIILTASSCLHGKEIRSMNEHVAQLYADLDGGFSHAAWLLPG : 239
XP_037650187 : FORWGDSGEKNLFVASELIIMTASSCLHGKEIRSMNEGVVAQLYADLDGGFSHAAWLLPG : 239
XP_031722207 : FORWGDSGERNLFVASELIILTASSCLHGKEIRSMLEKVAQLYADLDGGFSHAAWLLPG : 239

C. armatus : WLPLPSFRRRDRAHREIKNMFFYATQKRRTSNEKVDDEFLQTLIDATYKDGHSLSDDDEIAGL :
 Human : WLPLPSFRRRDRAHREIKDIFYKATQKRRSQSEKIDDLQTLIDATYKDGRLPLTDDDEVAGM : 304
 KAJ3609750 : WLPLPSFRRRDRAHREIKNIFFKATQKRRTSSEKVDDEFLQTLIDATYKDGHALSDDEIAGL : 300
 XP_030203989 : WLPLPSFRKRDRRAHREIKSMFFKATQKRRNSSEKGDDEFLQTLIDATYKDGHTLSDDDEISGL : 298
 XP_0564381 : WLPLPSFRKRDRRAHREIKSMFFKATQKRRNSSEKGDDEFLQTLIDATYKDGHTLSDDDEISGL : 298
 KAK0136477 : WVPLPSFRRRDRAHREIKNMFFKATQKRRTSKERVDDEFLQTLIDATYKDGHSLSDDDEIAGL : 297
 NP_001001730 : WLPLPSFRRRDRAHLEIKKIFYNVIKKREDTEKHDDILQTLIDATYKDGRLPLSDDEIAGM : 296
 XP_029591193 : WLPLPSFRRRDRAHREIKNIFYKVTQKRRSSGEKVDDMLQTLIDATYKDGRLPNDDEIAGM : 303
 XP_036948155 : WLPLPSFRKRDRRAHREIKNIFFKVIQKRRQSTEKVDDILQTLVDATYKNGRPLNDDDEIAGM : 301
 XP_010739985 : WLPLPSFRKRDRRAHREIKNIFFKVTQKRRSQSEKVDLQTLIDATYKDGRLPNDNEIAGM : 298
 KAF3707363 : WLPLPSFRKRDRRAHREIKNIFFKVIQKRRSGEKVDDILQTLIDATYKDGRLPLSDNEIAGM : 298
 QQL94751_1 : WLPLPSFRKRDRRAHREIKNIFFKVIQKRRSGEKVDDILQTLIDATYKDGRLPLSDNEIAGM : 300
 XP_039976906 : WLPLPSFRKRDRRAHREIKNIFFKVIQKRRSGEKVDDILQTLIDATYKDGQPLDDNEIAGM : 300
 XP_034066366 : WLPLPSFRKRDRRAHREIKNIFSKVTQKRRSQSEKVDLQTLIDATYKDGRLPNDSEIAGM : 300
 XP_033950401 : WLPLPSFRKRDRRAHREIKNIFSKVTQKRRSQSEKVDLQTLIDATYKDGRLPNDSEIAGM : 300
 XP_037650187 : WLPLPSFRKRDRRAHREIKNIFFKVIQKRRSQSEKVDMLQTLVDATYKDGQPLNNDNEIAGM : 300
 XP_031722207 : WLPLPSFRKRDRRAHTEIKNIFFKVIQKRRQSEKVDMLQTLVDATYKDGRLPNDNEISGM : 300

C. armatus : LIGLLLAGQHTSSTTSWMSFFFLARDKQLQERCLAEQKAVCGEDLPFLDFDQLKELSLDDR :
 Human : LIGLLLAGQHTSSTTSAWMGFFFLARDKTLQKKCLEQKTVCGENLPPLTYDQLKDLNLLDR : 365
 KAJ3609750 : LIGLLLAGQHTSSTTSWMTFFFLARDKQLQERCHAEQKAVCGDELPLEEDQLKDLGLDDR : 361
 XP_030203989 : LIGLLLAGQHTSSTTSAWMTFFFLARDKELQERCYAEQKAVCGEDLPLEEDQLKDLGLDDR : 359
 XP_0564381 : LIGLLLAGQHTSSTTSAWMTFFFLARDKELQERCYAEQKAVCGEDLPLEEDQLKDLGLDDR : 359
 KAK0136477 : LIGLLLAGQHTSSTTSWMTFFFLARDKELQERCYAEQKAVCGDDLPLEEDQLKDLSLDDR : 358
 NP_001001730 : LIGLLLAGQHTSSTTSAWMGFFFLARDKALQERCYAEQKAVCGEDLPFLHYDQLKDLSLDDR : 357
 XP_029591193 : LIGLLLAGQHTSSTTSWLGFFFLKDKALQDRCYAEQKTACGEDLPFLNFDQLKDLTLDDR : 364
 XP_036948155 : LIGLLLAGQHTSSTTSAWMGFFMAKDRSLQDRCYAEQKAVCGEALPFLDFDQLKDLSLDDR : 362
 XP_010739985 : LIGLLLAGQHTSSTTSWMGFFMARDKSLQERCYAEQKAACGEDLPFLDYDQLKDLNLLER : 359
 KAF3707363 : LIGLLLAGQHTSSTTSAWMGFFFLARDKDLQERCYAEQKTVCGEDLPFLDFDQLKDLSLLER : 359
 QQL94751_1 : LIGLLLAGQHTSSTTSAWMGFFFLARDKALQERCYAEQRAVCGEDLPFLDFDQLKDLSLLER : 361
 XP_039976906 : LIGLLLAGQHTSSTTSAWMGFFFLARDKALQERCYAEQRAVCGEDLPFLDFDQLKDLSLLER : 361
 XP_034066366 : LIGLLLAGQHTSSTTSAWMGFFFLARDKALQEKCYAEQKAVCGEDLPALDLDQLKDLSLLER : 361
 XP_033950401 : LIGLLLAGQHTSSTTSAWMGFFMAKDKALQEKCYAEQKAVCGEDLPALDLDQLKDLSLLER : 361
 XP_037650187 : LIGLLLAGQHTSSTTSWLGFFFLARDKALQERCYAEQRAVCGEELPFLDFDQLKDLSLLER : 361
 XP_031722207 : LIGLLLAGQHTSSTTSAWMGFFFLARDKALQERCYAEQRAVCGEGL-ELDFDQLKDLSLLER : 360

C. armatus : CLKETLRLRPPIMMMRMARSPOQVAGYTIPVGHQVCVSPTVNQRLPDSWTERDEFNPPRY :
 Human : CLKETLRLRPPIMMMRMARTPOQVAGYTIPVGHQVCVSPTVNQRLKDSWVERLDFNPPRY : 426
 KAJ3609750 : CVKETLRLRPPIMMMRLARSPOQVAGYTIPAGHQVCVSPTVNQRLPDTWTERHEFNPPRF : 422
 XP_030203989 : CVKETLRLRPPIMMMRMARSPOQVAGYTIPAGHQVCVSPTVNQRLPDTWTERDQFSPDRF : 420
 XP_0564381 : CVKETLRLRPPIMMMRMARSPOQVAGYTIPAGHQVCVSPTVNQRLPDTWTERDQFSPDRF : 420
 KAK0136477 : CVKETLRLRPPIMMMRMARSPOQVAGYTIPVGHQVCVSPTVNQRLPDTWTERDDFNPPRF : 419
 NP_001001730 : CLKETLRLRPPIMMMRMAKTPQKVGEYTIPVGHQVCVSPTVNHRLQDTWAERLDFDPPRY : 418
 XP_029591193 : CLKETLRLRPPIMMMRMARSPOQVAGYTIPAGHQVCVSPTVNHRLKDTWTERMEFNPPRY : 425
 XP_036948155 : CLKETLRLRPPIMMMRMARSPOQAAGYTIPVGHQVCVSPTVNHRLYDTWNERMEFNPPRY : 423
 XP_010739985 : CLKETLRLRPPIMMMRMARSPOQAAGYTIPVGHQVCVSPTVNHRLQDTWDKRLEFNPPRY : 420
 KAF3707363 : CLKETLRLRPPIMMMRMARSPOQAAGYTIPVGHQVCVSPTVNHRLHDTWVERMEFNPPRY : 420
 QQL94751_1 : CLKETLRLRPPIMMMRMARSPOQAAGYTIPVGHQVCVSPTVNHRLHDTWAERMEFNPPRY : 422
 XP_039976906 : CLKETLRLRPPIMMMRMARSPOQAAGYTIPVGHQVCVSPTVNHRLHDTWAERMEFNPPRY : 422
 XP_034066366 : CLKETLRLRPPIMMMRMARSLOQAAGYTIPVGHQVCVSPTVNQRLQDTWDERMEFSPDRY : 422
 XP_033950401 : CLKETLRLRPPIMMMRMARSLOQAAGYTIPVGHQVCVSPTVNQRLQDTWDERMEFSPDRY : 422
 XP_037650187 : CLKETLRLRPPIMMMRMARSPOQAAGYTIPVGHQVCVSPTVNQRLQDTWVERMEFSPDRY : 422
 XP_031722207 : CLKETLRLRPPIMMMRMARSPOQAAGYTIPVGHQVCVSPTVNQRLQDTWVERMEFSPDRY : 421

C. armatus : LNDNAATGEKFAYVPFGAGRHCIGENFAYVQLKTLSTLIRKFEFLVDGYFPTINFTTM :
 Human : LQDNPASGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTMLRLYEFDLVDGYFPTVNYTTM : 487
 KAJ3609750 : LNDNAASGDKFSYVPFGAGRHCIGENFAYVQLKTLSTMVRKYQFLVDGYFPTINFTTM : 483
 XP_030203989 : LSESAASGEKFAYVPFGAGRHCIGENFAYVQLKTLSTMTRAYEFLVDGYFPTINFTTM : 481
 XP_0564381 : LSESAASGEKFAYVPFGAGRHCIGENFAYVQLKTLSTMTRAYEFLVDGYFPTINFTTM : 481
 KAK0136477 : LNDNAASGEKFAYVPFGAGRHCIGENFAYVQLKTLSTMTRKYEFDLVDGYFPTINFTTM : 480
 NP_001001730 : LNDNPAAGEKFAYIPFGAGRHCIGENFAYVQIKTIWSTLLRMFDLVDGHPFPVNYTTM : 479
 XP_029591193 : LNDNPAAVEKFAYVPFGAGRHCIGENFAYVQIKTIWSTMLRLYEFDLVDGYFPTINFTTM : 486
 XP_036948155 : LNDNPAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTLLRMYDFDLVDGYFPTINFTTM : 484
 XP_010739985 : LNDNLAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTLLRMYDFDLVDGYFPTINFTTM : 481
 KAF3707363 : LNDNPAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTLLRMYEFDLVDGYFPTINFTTM : 481
 QQL94751_1 : LNDNPAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTLLRMYDFDLVDGYFPTINFTTM : 483
 XP_039976906 : LNDNPAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTLLRMYDFDLVDGYFPTINFTTM : 483
 XP_034066366 : LNDNPAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTLLRMYDFDLVDGYFPTINFTTM : 483
 XP_033950401 : LNDNPAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTLLRMYDFDLVDGYFPTINFTTM : 483
 XP_037650187 : LNDNPAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTMLRMYEFLVDGYFPTINFTTM : 483
 XP_031722207 : LNDNPAAGEKFAYVPFGAGRHCIGENFAYVQIKTIWSTLLRMYHFLVDGYFPTINFTTM : 482

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C.armatus      : IHTPHNPVIRYRSETH~~~~~ :
Human          : IHTPHNPVIRYKRESK~~~~~ : 503
KAJ3609750    : IHTPHNPFKICQTISCSAPVSRPRPSSPAAATGTTVMEDEERQKKLEAGKAK : 536
XP_030203989  : IHTPHNPVIRYRSEAR~~~~~ : 497
XP_056438121  : IHTPHNPVIRYRSEAH~~~~~ : 497
KAK0136477    : IHTPHNPVIRYKSETP~~~~~ : 496
NP_001001730  : IHTPHNPIIRYTRNTQPPQQ~~~~~ : 499
XP_029591193  : IHTPHNPVIRYKREQH~~~~~ : 502
XP_036948155  : IHTPHNPVIRYKREIQ~~~~~ : 500
XP_010739985  : IHTPHNPVIRYKRETKQ~~~~~ : 497
KAF3707363    : IHTPHNPFIRYKREKQ~~~~~ : 497
QQL94751_1    : IHTPHNPVIRYKREKP~~~~~ : 499
XP_039976906  : IHTPHTPVIRYKREKQ~~~~~ : 499
XP_034066366  : IHTPHNPVIKYKREAQ~~~~~ : 499
XP_033950401  : IHTPHNPIIKYKREAQ~~~~~ : 499
XP_037650187  : IHTPHNPIIRYKREKQ~~~~~ : 499
XP_031722207  : IHTPHNPVIRYQREKQ~~~~~ : 498

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Figure S1. Multiple sequence alignment of CYP51 proteins from fish and human.

KAJ3609750: *Muraenolepis orangiensis* (135 - 860 m); XP_030203989: *Gadus morhua* (up to 500-600m); XP_056438121: *Gadus chalcogrammus* (30-1300m); KAK0136477: *Merluccius polli* (50-910m); NP_001001730: *Danio rerio*; XP_029591193: *Salmo trutta*; XP_036948155: *Acanthopagrus latus*; XP_010739985: *Larimichthys crocea*; KAF3707363: *Channa argus*; QQL94751: *Lateolabrax maculatus*; XP_039976906: *Xiphias gladius*; XP_034066366: *Gymnodraco acuticeps*; XP_033950401: *Pseudochaenichthys georgianus*; XP_037650187: *Sebastes umbrosus*; XP_031722207: *Anarrhichthys ocellatus*.

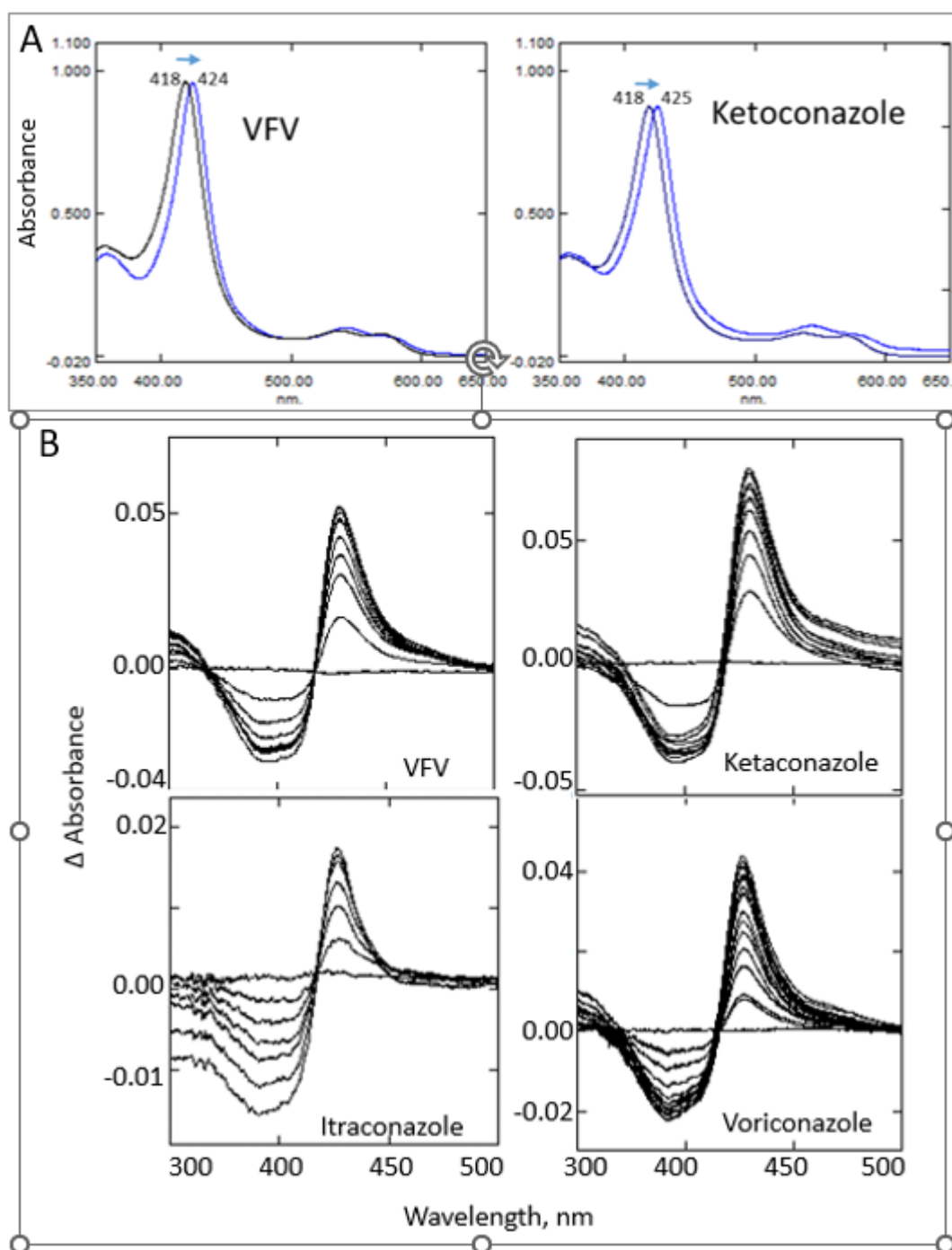


Figure S2. Spectral changes in *C. armatus* CYP51 in response to the addition of azoles. A. Absolute absorbance spectra. Black line - ligand-free, blue line - azole-bound protein sample. P450 concentration $\sim 8 \mu\text{M}$. **B.** Difference absorbance spectra upon titration (type II spectral response). P450 concentration $0.5 \mu\text{M}$, titration step $0.1 \mu\text{M}$.

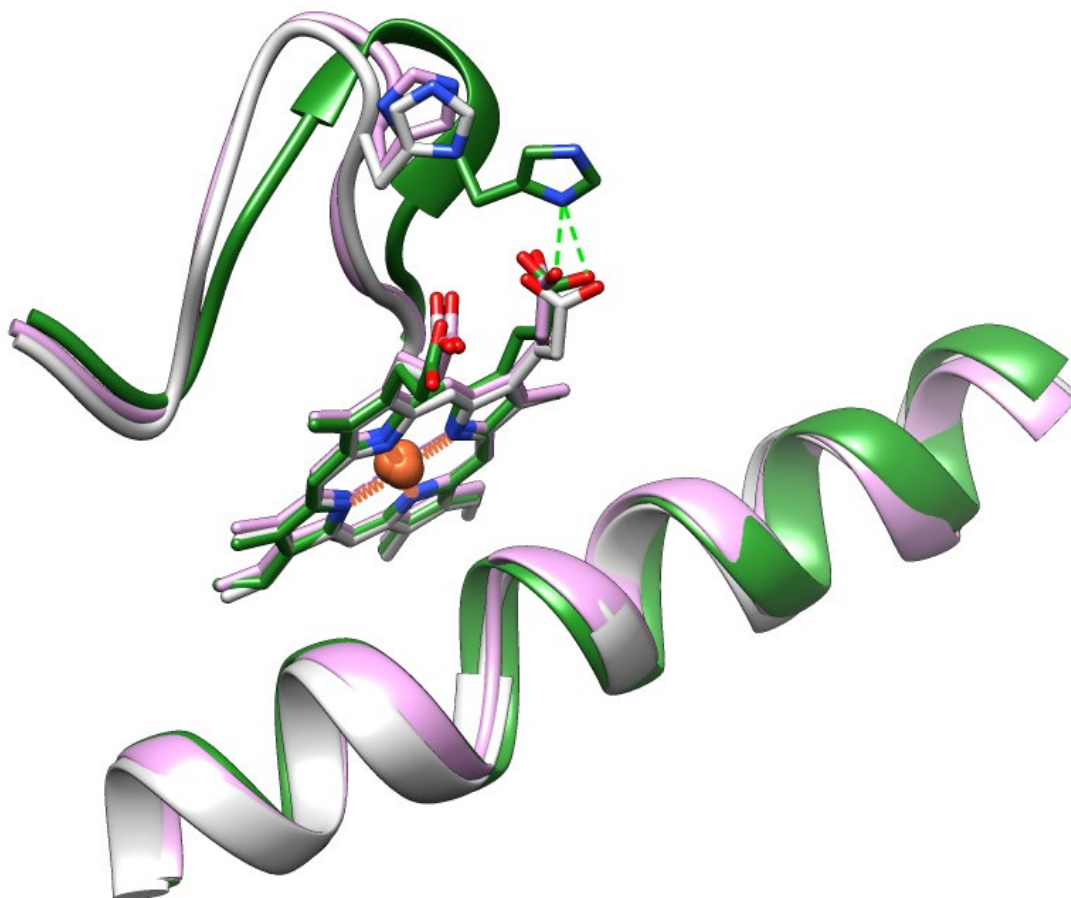


Figure S3. Helix I and the heme bulge in human CYP51 Alpha-Fold model AF-Q16850-F1 (green). Superimposed with human CYP51 (8SBI, plum) and *C. armatus* CYP51 (9BAT, grey).

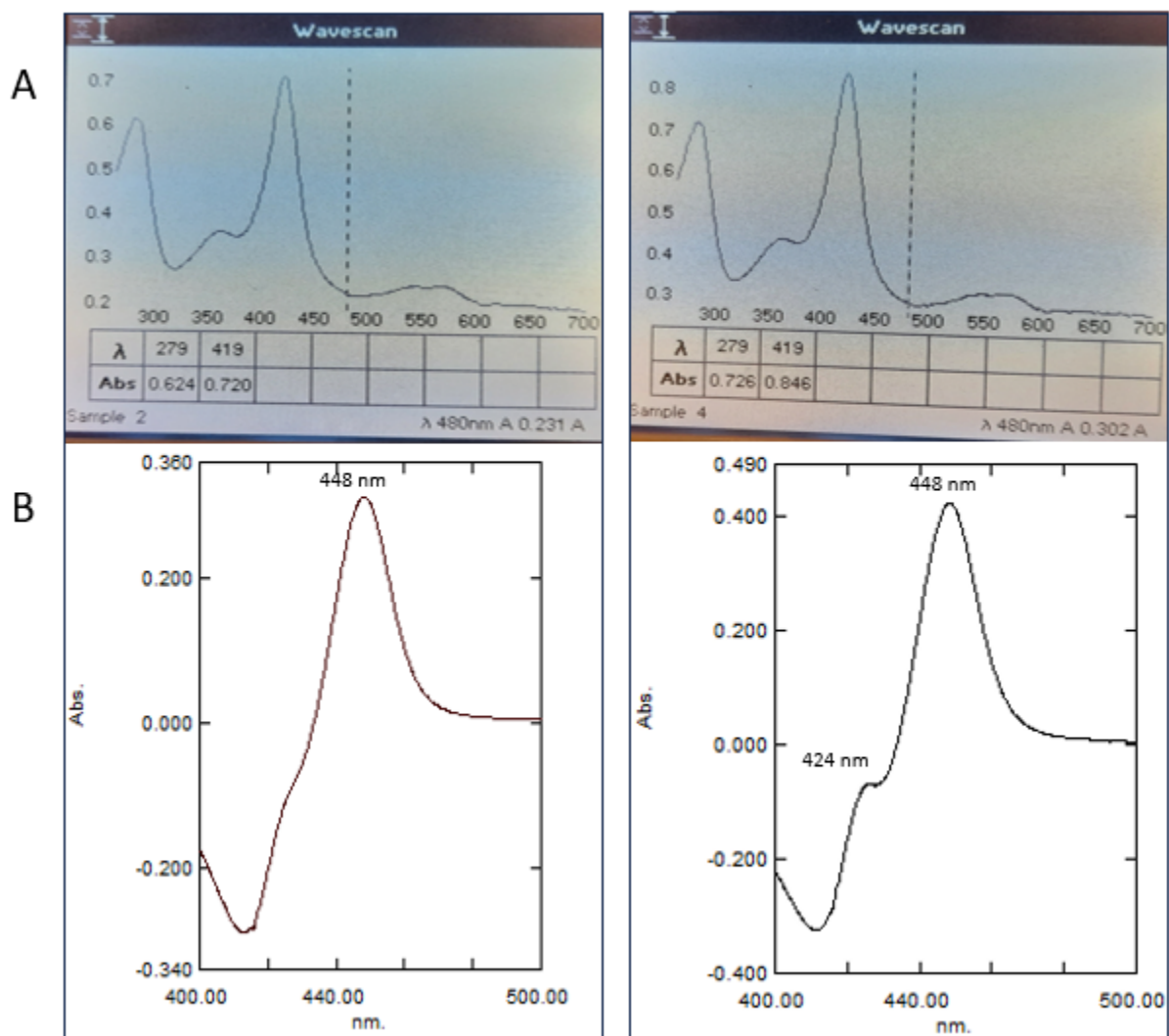


Figure S4. Absolute **(A)** and CO-binding difference **(B)** absorption spectra of the dissolved *C. armatus* CYP51 crystals (left panel), compared to the corresponding spectra of the protein sample used for crystallization (right panel).