

Supporting Information

Contents	Page
Methods	S2
Table S1. Linear Tyr/Trp Chain Search Results, 5-Å ET cutoff distance, ≥ 1 solvent-exposed residue	S2
Table S2. Branched Tyr/Trp Chain Search Results, 5-Å ET cutoff distance, ≥ 1 solvent-exposed residue.	S3
Table S3. Linear Tyr/Trp Chain Search Results, EC 1 Family, 5-Å ET cutoff distance, ≥ 1 solvent-exposed residue.	S4
Table S4. Sequence alignment of CYP11A1 proteins (from UniProt/Swiss-Prot database).	S6
Table S5. Linear Tyr/Trp Search Results, EC 3 Family, 5-Å ET cutoff distance, ≥ 1 solvent-exposed residue.	S8
Figure S1	S9
Figure S2	S10
Figure S3	S11
Figure S4	S11
Figure S5	S12
Figure S6	S12
Figure S7	S13
Figure S8	S13

Methods

Kinetics Simulations.

Tyr/Trp Chains used in Kinetics Simulations

CYP11A1 (PDB ID 3N9Y)

Tyr/Trp chain residues: TYR90; TYR93; TYR94; TRP87; TRP231

KDM4A (PDB ID 4V2W)

Tyr/Trp chain residues: TYR121; TYR209; TYR273; TYR275; TYR299; TRP122; TRP181; TRP187

Methane Monooxygenase Methylococcus capsulatus (Bath) (PDB ID 1MTY)

Linear Tyr/Trp chain residues: TYR251; TYR324; TRP313; TRP317

Branched Tyr/Trp chain residues: TYR292; TYR310; TYR340; TYR347; TYR351; TYR376; TYR380; TYR383; TYR-D387; TRP301; TRP305; TRP308; TRP341; TRP354; TRP371; TRP379; TRP390; TRP407; TRP507

Table S1. Linear Tyr/Trp Chain Search Results, 5-Å ET cutoff distance, ≥1 solvent-exposed residue

Maximum Chain Length (residues)		0	1	2	3	4	5	6	7	8	9	10	11	12
Data Set	Total Structures	Number of Structures with the Specified Chain Length (residues)												
Full DB	27,355	435	7741	10,600	5382	2100	686	257	90	43	13	7	0	1
EC 1	2200	6	516	863	505	198	57	32	11	6	0	6	0	0
EC 2	3590	22	969	1474	688	291	104	25	13	4	0	0	0	0
EC 3	3999	18	748	1495	976	440	183	80	36	15	8	0	0	0
EC 4	1024	6	306	401	215	70	18	5	2	1	0	0	0	0
EC 5	703	7	221	286	130	43	11	4	0	1	0	0	0	0
EC 6	703	6	160	304	166	49	13	3	2	0	0	0	0	0

Table S2. Branched Tyr/Trp Chain Search Results, 5-Å ET cutoff distance, ≥1 solvent-exposed residue

Maximum Chain Length (residues)		0	1	2	3	4	5	6	7	8	9	10	11	12
Data Set	Total Structures	Number of Structures with the Specified Chain Length												
Full DB	27,355	435	7741	9869	4987	2334	1018	473	208	129	68	34	23	13
EC 1	2200	6	516	791	452	232	100	42	19	16	12	3	2	3
EC 2	3590	22	969	1381	630	304	155	74	26	14	10	3	2	0
EC 3	3999	18	748	1364	872	466	242	117	58	47	29	15	15	4
EC 4	1024	6	306	377	196	78	38	13	6	1	1	1	1	0
EC 5	703	7	221	266	124	53	19	8	4	0	0	0	1	0
EC 6	703	6	160	293	151	58	22	8	3	0	1	0	0	0

Table S2. Branched Tyr/Trp Chain Search Results, 5-Å ET cutoff distance, ≥1 solvent-exposed residue (continued)

Maximum Chain Length (residues)	13	14	15	16	17	18	19	20	21	22	23
Data Set	Number of Structures with the Specified Chain Length										
Full DB	6	4	3	1	1	3	3	1	0	0	1
EC 1	1	0	0	0	0	2	2	1	0	0	0
EC 2	0	0	0	0	0	0	0	0	0	0	0
EC 3	2	1	1	0	0	0	0	0	0	0	0
EC 4	0	0	0	0	0	0	0	0	0	0	0
EC 5	0	0	0	0	0	0	0	0	0	0	0
EC 6	1	0	0	0	0	0	0	0	0	0	0

Table S3. Linear Tyr/Trp Chain Search Results, EC 1 Family, 5-Å ET cutoff distance, ≥1 solvent-exposed residue

Maximum Chain Length (residues)		0	1	2	3	4	5	6	7	8	9	10
Data Set	Total Structures	Number of Structures with the Specified Chain Length										
EC 1	2200	6	516	863	505	198	57	32	11	6	0	6
EC 1.1	576	0	167	239	120	34	10	6	0	0	0	0
EC 1.2	175	0	44	70	46	12	2	1	0	0	0	0
EC 1.3	160	0	34	71	30	16	4	3	2	0	0	0
EC 1.4	83	0	7	30	28	11	4	2	1	0	0	0
EC 1.5	107	0	24	35	38	8	2	0	0	0	0	0
EC 1.6	69	1	15	29	17	6	1	0	0	0	0	0
EC 1.7	69	0	13	22	18	8	1	2	1	1	0	3
EC 1.8	150	1	39	56	39	11	3	1	0	0	0	0
EC 1.8	13	0	0	2	4	2	0	5	0	0	0	0
EC 1.10	59	0	11	19	7	14	4	0	4	0	0	0
EC 1.11	150	0	62	51	27	8	1	0	0	1	0	0
EC 1.12	19	0	1	8	4	3	3	0	0	0	0	0
EC 1.13	98	0	11	38	30	12	7	0	0	0	0	0
EC 1.14	254	0	30	101	77	30	7	3	1	2	0	3
EC 1.15	84	4	22	18	3	15	8	9	4	1	0	0
EC 1.16	35	0	11	15	5	2	0	2	0	0	0	0
EC 1.17	52	0	8	21	12	10	1	0	0	0	0	0
EC 1.18	35	0	8	17	9	1	0	0	0	0	0	0
EC 1.20, 21,22,97	22	0	7	7	5	1	1	0	0	1	0	0

Definitions:

- EC 1 Oxidoreductases
- EC 1.1 Acting on the CH-OH group of donors
- EC 1.2 Acting on the aldehyde or oxo group of donors
- EC 1.3 Acting on the CH-CH group of donors
- EC 1.4 Acting on the CH-NH₂ group of donors
- EC 1.5 Acting on the CH-NH group of donors
- EC 1.6 Acting on NADH or NADPH
- EC 1.7 Acting on other nitrogenous compounds as donors
- EC 1.8 Acting on a sulfur group of donors
- EC 1.9 Acting on a heme group of donors
- EC 1.10 Acting on diphenols and related substances as donors
- EC 1.11 Acting on a peroxide as acceptor
- EC 1.12 Acting on hydrogen as donor
- EC 1.13 Acting on single donors with incorporation of molecular oxygen
- EC 1.14 Acting on paired donors, with incorporation or reduction of molecular oxygen

EC 1.15 Acting on superoxide as acceptor
EC 1.16 Oxidizing metal ions
EC 1.17 Acting on CH or CH₂ groups
EC 1.18 Acting on iron-sulfur proteins as donors
EC 1.19 Acting on reduced flavodoxin as donor
EC 1.20 Acting on phosphorus or arsenic in donors
EC 1.21 Catalyzing the reaction $X-H + Y-H = X-Y$
EC 1.22 Acting on halogen in donors
EC 1.23 Reducing C-O-C group as acceptor
EC 1.97 Other oxidoreductases

Table S4. Sequence alignment of CYP11A1 proteins (from UniProt/Swiss-Prot database). Positions of human residues Trp87 (yellow), Tyr90 (green), Tyr93 (cyan), Tyr94 (magenta), and Trp231 (red) are highlighted in color.

CP11A_HUMAN	-----MLAKGLPPRSVL-VKGCQTFLSAPREGLGRLRVPTGEGAGIS-TRSPRPFPNEIPS	53
CP11A_RAT	-----MLAKGLCLRSVL-VKSCQPFLSPVWQ--GPGLATGNGAGISSTNSPRSPNEIPS	51
CP11A_MESAU	-----MLAKGLSLRSVL-AGKGCQPFLSPTWQ---SSVLATGGGANIS-TNSPRFPNEIPS	50
CP11A_MOUSE	-----MLAKGLSLRSVL-VKGCQPFLSPTWQ---GPVLSTGKGAGTS-TSSPRSPNEIPS	50
CP11A_MACFA	-----MLAKGLPPRSVL-VKGCQTFLSAPKERLGLHLRVPTSEGAGIS-TRSPRPFPNEIPS	53
CP11A_BOVIN	-----MLARGLPLRSAL-VKACPPILSTVGEWGHHRVGTGEGAGIS-TKTPRPYSEIPS	53
CP11A_SHEEP	-----MLARGLPFRSAL-VKACPLLNTGREWGHHRVGTGEGAGIS-TRTPRPYSEIPS	53
CP11A_PIG	-----MLARGLPLRSVL-VKGCQPFLSAPRECPGHPRVGTGEGACIS-TKTPRPFSEIPS	53
CP11A_HORSE	-----MLVRGLPLRSVL-VKGCQPFLSAPREGPGHPRVPTGEGAGMS-SHSPRPFKSEIPS	53
CP11A_CAPHI	-----MLARGLPLRSAL-VKACPLLNTGREWGHHRVGTGEGAGIS-TRTPRPYSEIPS	53
CP11A_RABIT	-----RGLPSRSVF-LRGCQASLSTAQERLGHVPTREGVVA-TRSPRPYHEIPS	50
CP11A_DASAM	SFRLSLSASTYAQRGSFTTPEHDFTLFPHRN---H--SVTSESRIPESEQLKSLTDIPG	54
CP11A_ONCMY	-----MMVSVSVCRSSALPACGLPSARHNS---SMPVVRQALSPDNSSSTVQNFSEIPG	51
CP11A_HUMAN	PGDNGWLNLYHFWRGTGTHKVLHHVQNFQYKGPYREKLGNVESVYVIDPEDVALLFKS	113
CP11A_RAT	PGDNGWINLYHFLRENGTHR IYHHMQNFQYKGPYREKLGNMESVYILDPKDAATLFSC	111
CP11A_MESAU	PGDNGWLNLYHFWRENGTHR IYHHMQNFQYKGPYREKLGKNDKSVYILDPEAAQLFSL	110
CP11A_MOUSE	PGDNGWLNLYHFWRSGTQKIHYHQMSFQYKGPYREKLGTLSEVYIVDPKDAIILFSC	110
CP11A_MACFA	PGDNGWLNLYHFWRGTGTHKVLHHVQNFQYKDPYREKLGNVESVYVIDPEDVALLFKS	113
CP11A_BOVIN	PGDNGWLNLYHFWRKKSQR IHFHRIENFQYKGPYREKLGKNDKSVYIHPEDVAHLFKF	113
CP11A_SHEEP	PGDNGWINLYHFWRKKSQR IHFHRIENFQYKGPYREKLGKNDKSVYIHPEDVAHLFKF	113
CP11A_PIG	PGDNGWINLYHFWRKKSQR IHFHRIENFQYKGPYREKLGKNDKSVYIHPEDVAHLFKF	113
CP11A_HORSE	PGDNGWINLYHFWRKKSQR IHFHRIENFQYKGPYREKLGKNDKSVYIHPEDVAHLFKF	113
CP11A_CAPHI	PGDNGWINLYHFWRKKSQR IHFHRIENFQYKGPYREKLGKNDKSVYIHPEDVAHLFKF	113
CP11A_RABIT	PGDNGWLNLYHLAEKGTGTHVYRHVQNFQYKGPYREKLGKNDKSVYIHPEDVALLFNS	110
CP11A_DASAM	NWRKNWLVVYFWRSNGLNNAHQWMLDNFNKYGPIYREKIAYYESINIINPADAVIMNKS	114
CP11A_ONCMY	LWRNGLANLYSFWKLDGFRNIHRVMVHNFNTFGPIYREKIGYYSVNI IKPEMPAILFKA	111
CP11A_HUMAN	EGPNPERFLIPPWVAHQYQRPVGVLLKKSAAWKDRVALNQEVMAPETKFNFLPLLDA	173
CP11A_RAT	EGPNPERYLPPWVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPDSIKNFVPLLEG	171
CP11A_MESAU	EGPYPERYLPPWVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPETKFNFLPLLEG	170
CP11A_MOUSE	EGPNPERFLIPPWVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPGAIKNFVPLLEG	170
CP11A_MACFA	EGPNPERFLIPPWVAHQYQRPVGVLLKKSAAWKDRVALNQEVMAPETKFNFLPLLDA	173
CP11A_BOVIN	EGSYPERYDIPPLVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPETKFNFLPLLNP	173
CP11A_SHEEP	EGSYQORYDIPPLVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPETKFNFLPLLNP	173
CP11A_PIG	EGPNPERYNIPPWVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPETKFNFLPLLD	173
CP11A_HORSE	EGPHPERFLIPPWVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPETKFNFLPLLD	173
CP11A_CAPHI	EGSYQORYDIPPLVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPETKFNFLPLLNP	173
CP11A_RABIT	EGPQPERFLIPPWVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPDAIKNFVPLLEA	170
CP11A_DASAM	EGPFPKRIEMAPWVAHQYQRPVGVLLKKSAAWKDRVILNQEVMAPDAIKNFVPLFNE	174
CP11A_ONCMY	EGHYPKRLTVEAWTSRDYRNRKYGVLLKNGEDWRSNRVILNREVISPKVLGNFVPLLDE	171
CP11A_HUMAN	VSRDFVSVLHRRIKKAGSGNYSGDISDDLFRFAPESITNVI FGERQGMLEEVVNPEAQR	233
CP11A_RAT	VAQDFIKVLHRRIKQKNSGKFSGDISDDLFRFAPESITSVVFGERLGMLEEIVDPESQRF	231
CP11A_MESAU	VQQDFINVLHRRIKQKNSGKFSGDISDDLFRFAPESITSVVFGERLGMLEEIVDPESQRF	230
CP11A_MOUSE	VAQDFIKVLHRRIKQKNSGKFSGDISDDLFRFAPESISSVI FGERMGMLEEIVDPEAQR	230
CP11A_MACFA	VSRDFVSVLHRRIKKAGSGNYSGDISDDLFRFAPESITNVI FGERQGMLEEVVNPEGQRF	233
CP11A_BOVIN	VSQDFVSVLLHRRIKQKNSGKFSGDIKEDLFRFAPESITNVMFGERLGMLEETVNPEAQKF	233
CP11A_SHEEP	VSQDFVSVLLHRRIKQKNSGKFSGDIKEDLFRFAPESITNVMFGERLGMLEETVDTTEAQKF	233
CP11A_PIG	VSQDFVSVLHRRIKQKNSGKFSGDIREDLFRFAPESITNVI FGERLGMLEEIVDPEAQKF	233
CP11A_HORSE	VSQDFVSVLLHRRMEQKNSGKFSGPIIEDLFRFAPESITNVI FGERQGMLEIVDPEAQRF	233
CP11A_CAPHI	VSQDFVSVLLHRRIKQKNSGKFSGDIKEDLFRFAPESITNVMFGERLGMLEETVNTEAQKF	233
CP11A_RABIT	VSQAFVSMVHGRVQ---QGVFSGDISDDLFRFAPESMTNIMFGERLGMLEETVDPPEAHEF	227
CP11A_DASAM	VVLDFVSMVHKEVEKRSRSDYKTDLTNDLFLKALEVICYILYGERLDLLQRKYNKAPQKF	234
CP11A_ONCMY	VQDFVARVHKKIERSGQDKWTTDLSQELFKYALESVGSVLYGERLGLMLDYINPEAQHF	231
CP11A_HUMAN	IDAIYQMFHTSVPMNLNPPDLFRLFRKTWTDHVAADVI FSKADIYQNFYWELRQKGS	293
CP11A_RAT	IDAVYQMFHTSVPMNLNPPDLFRLFRKTWTDHAAAADVI FSKADEYTQNFYWDLRQKRD	291
CP11A_MESAU	IDAIYQMFHTSVPMNLNPPDLFRLFRKTWTDHAAAADMI FKKADYDTQTFYWDLRQKQE	290
CP11A_MOUSE	INAVYQMFHTSVPMNLNPPDFRLLRKTWTDHAAAADVI FNKADEYTQNFYWDLRQKRD	290
CP11A_MACFA	IDAIYQMFHTSVHMLNLPDLFRLFRKTWTDHVAADVI FSKADMYTENFHWELRQKGN	293
CP11A_BOVIN	IDAVYKMFHTSVPLNLPPELYRFLFRKTWRDHVAADTI FNKAKEYTEIFYQDLRRKTE	293
CP11A_SHEEP	IDAVYKMFHTSVPLNLPPELYRFLFRKTWRDHVAADTI FNKAKEYTEIFYQDLRQKTE	293
CP11A_PIG	IDAVYQMFHTSVPMNLNPPDLFRLFRKTWRDHVAADTI FNKAKEYTQNFYWDLRRKRE	293
CP11A_HORSE	IDAVYKMFHTSVPMNLPDLFRLFRKTWRDHVAADTVFSKAEQYTEKFYQDLRQKRD	293
CP11A_CAPHI	IDAVYKMFHTSVPLNLPPELYRFLFRKTWRDHVAADTI FNKAKEYTEIFYQDLRQKTE	293
CP11A_RABIT	IDAVYQMFHTSVPMNLPDLFRLFRKTWRDHVAADVI FTNADKYTQSFYWDLRQKQD	287
CP11A_DASAM	IDSIAATMFHSTPIMLYVPPSLKINSKIQQHVGSDNI FEHADTYLKKAYRQFQGSK	294
CP11A_ONCMY	IDCISLMFKTTPMPLYIPPAMLRRVGAKIWRDHVAADGIFNQADRCIQNIYRTMRQDTN	291

CP11A_HUMAN	VHHDYRGILYRLLGDSKMSFEDIKANVTEMLAGGVDTTSMTLQWHLYEMARNLKVQDMLR	353
CP11A_RAT	-FSKYPGVLYSLLGKNKLPFKNIQANITEMLAGGVDTTSMTLQWNLYEMAHNLKVQEMLR	350
CP11A_MESAU	-FSKYPGVLYSLLGKNKLPFKNIQANITEMLAGGVDTTSMTLQWLSYEMAHNLKVQEMLR	349
CP11A_MOUSE	-FSQYPGVLYSLLGKNKLPFKNIQANITEMLAGGVDTTSMTLQWNLYEMAHNLKVQEMLR	349
CP11A_MACFA	VHHDYRGILYRLLGDSKMSFEDIKANVTEMLAGGVDTTSMTLQWHLYEMARNLKVQDMLR	353
CP11A_BOVIN	-FRNYPGILYCLLKSEKMLLEDVKANITEMLAGGVNTTSMTLQWHLYEMARSLNVQEMLR	352
CP11A_SHEEP	-FRNYPGILYHLLKSEKMLLEDVKANITEMLAGGVDTTSMTLQWHLYEMARSLNVQEMLR	352
CP11A_PIG	-FNNYPGILYRLLGNDKLLSEVDKANVTEMLAGGVDTTSMTLQWHLYEMARSLNVQEMLR	352
CP11A_HORSE	-FDSYPGIFYRLLASNKLPFKDIQANVTEMLAGGVDTTSMTLQWHLYEIARNLRVQEMLR	352
CP11A_CAPHI	-FRNYPGILYHLLKSEKMLLEDVKANITEMLAGGVDTTSMTLQWHLYEMARSLNVQEMLR	352
CP11A_RABIT	LGGSYRGILYSLLTGSKLSFEDIKANVTEMLAGSVDTTSMTLQWHLYEMGAALGHQEMLR	347
CP11A_DASAM	NEHAFPGVLTLLQALPFEDIRASIDVMSGADTTSTTVHMMYELAKHPHIQKNVR	354
CP11A_ONCMY	THGKYPGVLASLLMLDKLSIEDIKASVTEMLAGGVDTTSTLLWTLYELARHPDLQEEELR	351
CP11A_HUMAN	AEVLAARHQAGQDMATMLQVPLLKASIKETLRLHPISVTLQRYLVNDLVLRDYMIPAKT	413
CP11A_RAT	AEVLAARRQAQGDMAKMQVPLLKASIKETLRLHPISVTLQRYIVNDLVLRNYKIPAKT	410
CP11A_MESAU	AEVLAARRQAQGDMAKMQVPLLKASIKETLRLHPISVTVQRYLVDDLVLRNYRIPAKM	409
CP11A_MOUSE	AEVLAARRQAQGDMAKMQVPLLKASIKETLRLHPISVTLQRYTVNDLVLRNYKIPAKT	409
CP11A_MACFA	AEVLAARRQAQGDMATILQVPLLKASIKETLRLHPISVTLQRYLVNDLVLRGYMIPAKT	413
CP11A_BOVIN	EEVLNARRQAEGDISKMLQMVPLLKASIKETLRLHPISVTLQRYPESDLVLQDYLIPAKT	412
CP11A_SHEEP	KEVLNARRQAEGDISKMLQMVPLLKASIKETLRLHPISVTLQRYPESDLVLQDYLIPAKT	412
CP11A_PIG	EEVLNARRQAQGDTSKMLQVPLLKASIKETLRLHPISVTLQRYLVNDLVLRDYMIPAKT	412
CP11A_HORSE	EEVLAARRQAQGDSTMVQMVPLLKASIKETLRLHPISVTLQRYVNDLVLRDYMIPAKT	412
CP11A_CAPHI	EEVLNARRQAEGDISKMLQMVPLLKASIKETLRLHPISVTLQRYPESDLVLQDYLIPAKT	412
CP11A_RABIT	AEVLAARRQAQGDMTAMLSVPLLKASIKETLRLHPISVTLQRYLVNDLVLQDYMIPAKT	407
CP11A_DASAM	SEIMEAHQKTEGDPVKMLKSVPLLKCVVKTLLRYPVAISIQRYLNETVQLQNYHIPAGT	414
CP11A_ONCMY	AEVAVARQSTQGDMLQMLKMIPLVKGALKETLRLHPVAVSLQRYITEEIIVIQNYHIPCGT	411
CP11A_HUMAN	LVQVAIYALGREPTFFFDPENFDPTRWLSKDKNITYFRNLGFGWGVRCQCLGRRIAELEM	473
CP11A_RAT	LVQVASIAMGRESSFFPNPNKFDPTRWLEKSQNTTHFRYLGFGWGVRCQCLGRRIAELEM	470
CP11A_MESAU	LVQVANYAMGREPSFFPNPNKFDPTRWLEKSQNTTHFRYLSFGWGVRCQCLGRRIAELEM	469
CP11A_MOUSE	LVQVASFAMGRDPGFFPNPNKFDPTRWLEKSQNTTHFRYLGFGWGVRCQCLGRRIAELEM	469
CP11A_MACFA	LVQVAIYALGREPTFFFDPENFDPTRWLSKDKNITYFRNLGFGWGVRCQCLGRRIAELEM	473
CP11A_BOVIN	LVQVAIYAMGRDPAFFSSPDKFDPTRWLSKDKDLIHFRNLGFGWGVRCQCVGRRIAELEM	472
CP11A_SHEEP	LVQVAIYAMGRDPAFFSNPDKFDPTRWLGKDKDLIHFRNLGFGWGVRCQCVGRRIAELEM	472
CP11A_PIG	LVQVAIYAMGRDPAFFSNPDKFDPTRWLGKDKDLIHFRNLGFGWGVRCQCVGRRIAELEM	472
CP11A_HORSE	LVQVSIYTMGQDPTFFSNPRFDPTRWLDKDKDLIHFRNLGFGWGVRCQCLGRRIAELEM	472
CP11A_CAPHI	LVQVAIYAMGRDPAFFSNPDKFDPTRWLGKDKDLIHFRNLGFGWGVRCQCVGRRIAELEM	472
CP11A_RABIT	LVQVANYGMGREPSFFANPEKFDPPRWLDKDKNATHFR-----	445
CP11A_DASAM	LVQLGLYAMGRNPKIFKNPEQYNPERWLKGE--DTHFRHLGFGFGPRQCIGRRIAETQMV	472
CP11A_ONCMY	LVQLGLYAMGRDPPVFRPEKYLPSRWLRTE--NQYFRSLGFGFGPRQCIGRRIAETEMQ	469
CP11A_HUMAN	I FLINMLENFRVEIQHLSVDVGTTFNLILMPEKPI SFTFWPFNQEATQQ-----	521
CP11A_RAT	I FLINVLENFRIEVSQIRDVGTGTFNLILMPEKPI FNFQPLKQDLGSTMPRKGDTV-	526
CP11A_MESAU	I FLINVLENFRIELQSLHDVGTGTFNLILMPEKPI FLNLQPLKDKLGTTTNR-----	520
CP11A_MOUSE	I LLINLLENFRIEVOQLRDVGTGTFNLILMPEKPI LFNQPLKQDLGPAVTRKDNVTN	526
CP11A_MACFA	I FLINMLENFRVEIQHLSVDVGTTFNLILMPEKPI SFTFWPFNQEATQE-----	521
CP11A_BOVIN	LFLIHILENFKVEMQHIGDVNTIFNLILTPDKPI FLVFRPFNQDPPQA-----	520
CP11A_SHEEP	LFLIHILENFRVEMQQIGDVNTIFNLILTPDKPI FLVFRPFNQDPPQA-----	520
CP11A_PIG	LFLIHILENFKVELQHFSDVNTIFNLILMPEKPI FLVFRPFNQDPLQA-----	520
CP11A_HORSE	LFLIHILENFRVEIQHLDVSTFGLILIPKPI SFTFWPI TRAPPQA-----	520
CP11A_CAPHI	LFLIHILENFKIEMQQIGDVNTIFNLILTPDKPI FLVFRPFNQDPPQA-----	520
CP11A_RABIT	-----	-----
CP11A_DASAM	LLMIHMLQNFKIETDPMTEVKSFKSLILIPDKPINLKFTPIK-----	514
CP11A_ONCMY	LFLIHMLENFRVDKQRQVEVHSTFELILLPEKPI LLTLKPLKSGQ-----	514

The organisms are as follows:

CP11A_HUMAN	<i>Homo sapiens (Human)</i>
CP11A_RAT	<i>Rattus norvegicus (Rat)</i>
CP11A_MESAU	<i>Mesocricetus auratus (Golden hamster)</i>
CP11A_MOUSE	<i>Mus musculus (Mouse)</i>
CP11A_MACFA	<i>Macaca fascicularis (Crab-eating macaque) (Cynomolgus monkey)</i>
CP11A_BOVIN	<i>Bos taurus (Bovine)</i>
CP11A_SHEEP	<i>Ovis aries (Sheep)</i>
CP11A_PIG	<i>Sus scrofa (Pig)</i>
CP11A_HORSE	<i>Equus caballus (Horse)</i>
CP11A_CAPHI	<i>Capra hircus (Goat)</i>
CP11A_RABIT	<i>Oryctolagus cuniculus (Rabbit)</i>
CP11A_DASAM	<i>Dasyatis americana (Southern stingray)</i>
CP11A_ONCMY	<i>Oncorhynchus mykiss (Rainbow trout) (Salmo gairdneri)</i>

Table S5. Linear Tyr/Trp Search Results, EC 3 Family, 5-Å ET cutoff distance, ≥1 solvent-exposed residue

Maximum Chain Length (residues)		0	1	2	3	4	5	6	7	8	9
Data Set	Total Structures	Number of Structures with the Specified Chain Length									
EC 3	3999	18	748	1495	976	440	183	80	36	15	8
EC 3.1	1225	4	248	533	275	105	44	9	7	0	0
EC 3.2	863	1	61	172	241	178	107	62	24	11	6
EC 3.3	27	0	2	17	5	3	0	0	0	0	0
EC 3.4	1144	5	180	462	327	116	35	9	4	4	2
EC 3.5	470	1	121	201	105	33	7	1	1	0	0
EC 3.6	582	7	168	268	106	29	4	0	0	0	0
EC 3.7	16	0	3	6	6	0	1	0	0	0	0
EC 3.8	32	0	5	18	8	0	1	0	0	0	0
EC 3.9,10 11,13	8	0	4	2	1	1	0	0	0	0	0

Definitions:

EC 3 Hydrolases

EC 3.1 Acting on ester bonds

EC 3.2 Glycosylases

EC 3.3 Acting on ether bonds

EC 3.4 Acting on peptide bonds (peptide hydrolases)

EC 3.5 Acting on carbon-nitrogen bonds, other than peptide bonds

EC 3.6 Acting on acid anhydrides

EC 3.7 Acting on carbon-carbon bonds

EC 3.8 Acting on halide bonds

EC 3.9 Acting on phosphorus-nitrogen bonds

EC 3.10 Acting on sulfur-nitrogen bonds

EC 3.11 Acting on carbon-phosphorus bonds

EC 3.12 Acting on sulfur-sulfur bonds

EC 3.13 Acting on carbon-sulfur bonds

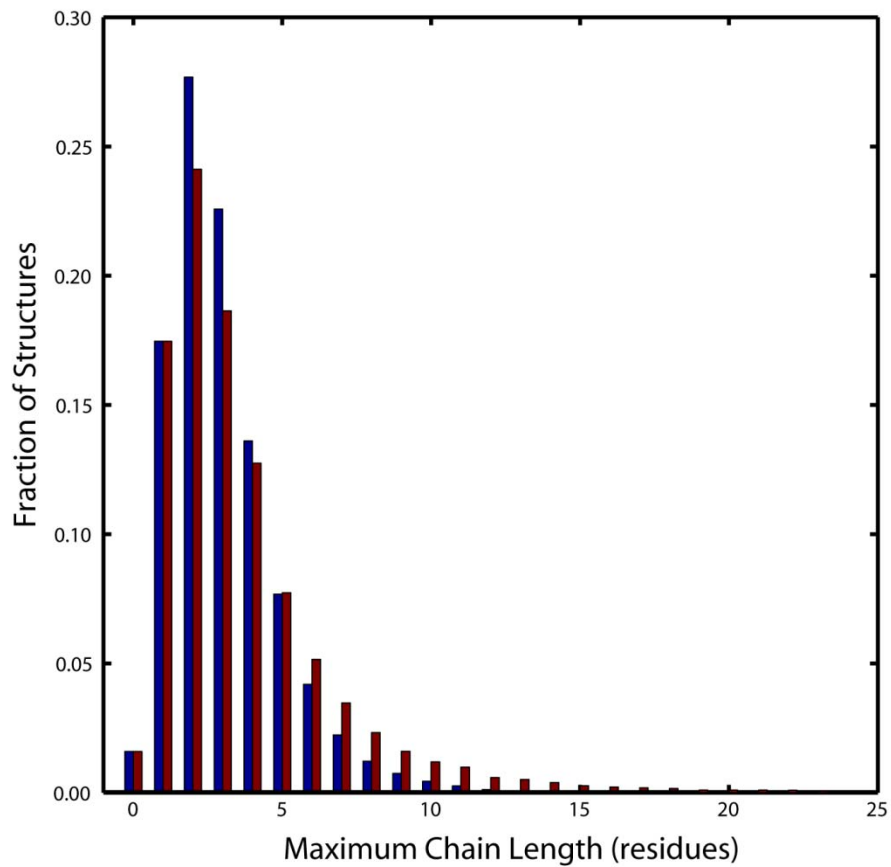


Fig. S1. Distributions of maximum linear (blue) and branched (red) redox chain lengths (7.5-Å ET cutoff, at least one solvent-exposed residue) found in 27,355 unique protein x-ray crystal structures in the RCSB Protein Data Bank (mean linear chain (MLC) 3.02 residues, 54% of structures with maximum linear chain length ≥ 3 residues; mean branched chain (MBC) 3.71 residues, 57% of structures with maximum branched chain length ≥ 3 residues).

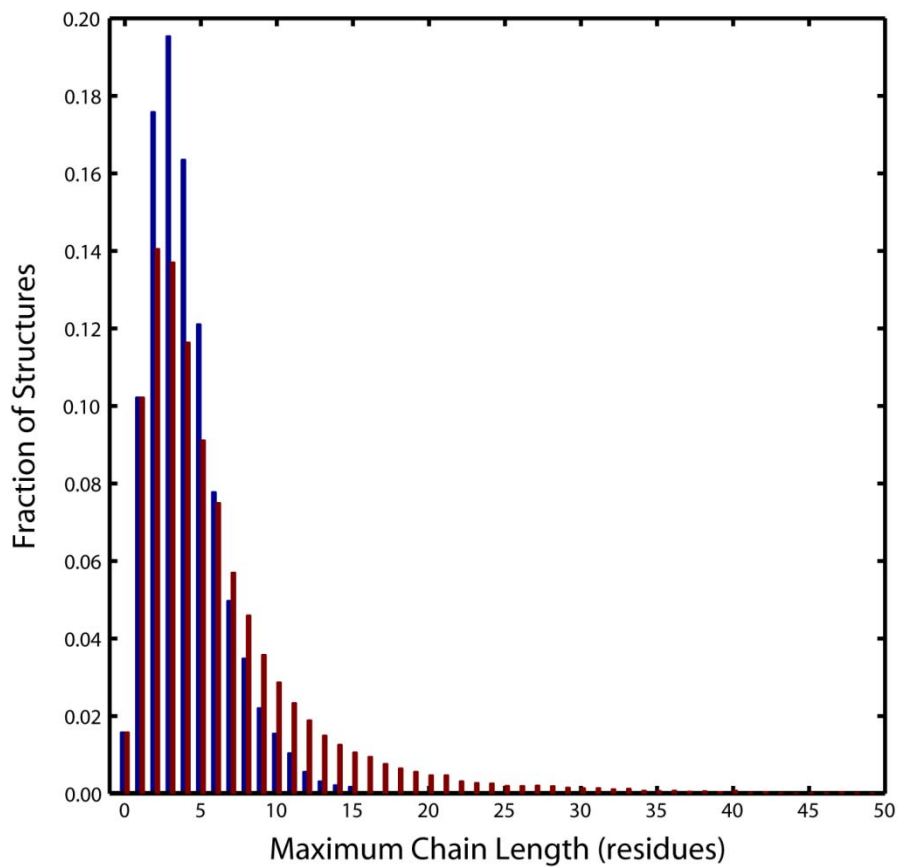
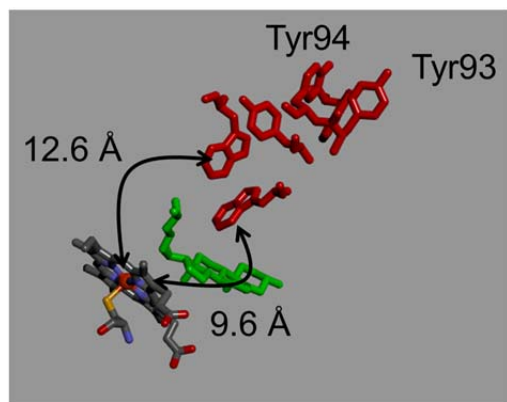


Fig. S2. Distributions of maximum linear (blue) and branched (red) redox chain lengths (10-Å ET cutoff, at least one solvent-exposed residue) found in 27,355 unique protein x-ray crystal structures in the RCSB Protein Data Bank (MLC 4.07 residues, 71% of structures with maximum linear chain length ≥ 3 residues; MBC 6.30 residues, 74% of structures with maximum branched chain length ≥ 3 residues).



(CYP11A1, PDB #3N9Y)

Fig. S3. Active site and Tyr/Trp chain residues in CYP11A1.

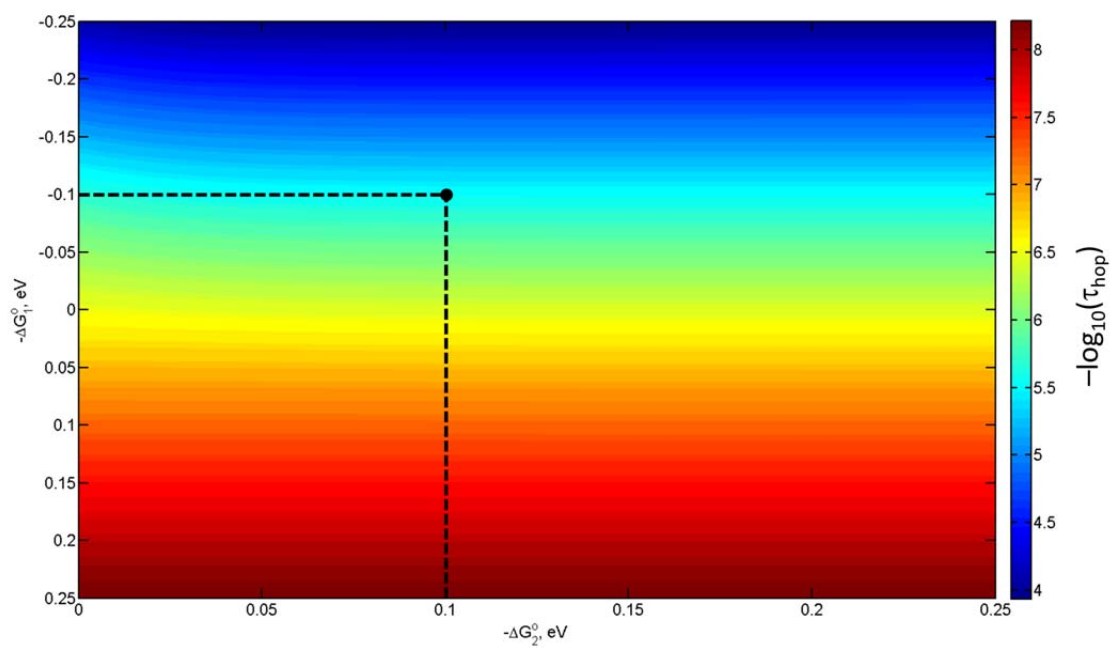
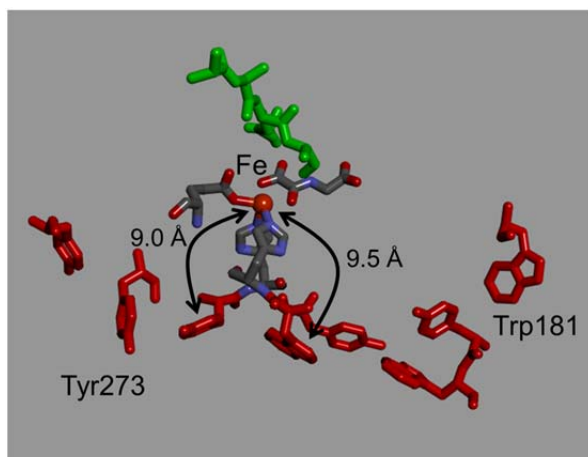


Fig. S4. Electron hopping map for Tyr/Trp chain in CYP11A1. Color indicates survival time (τ_{hop} , seconds) of a hole at the origin residue. Intersection of the dashed lines indicates location of estimated survival time point ($\sim 3 \mu\text{s}$).



KDM4A, PDB ID 4V2W

Fig. S5. Active site and Tyr/Trp chain residues in KDM4A.

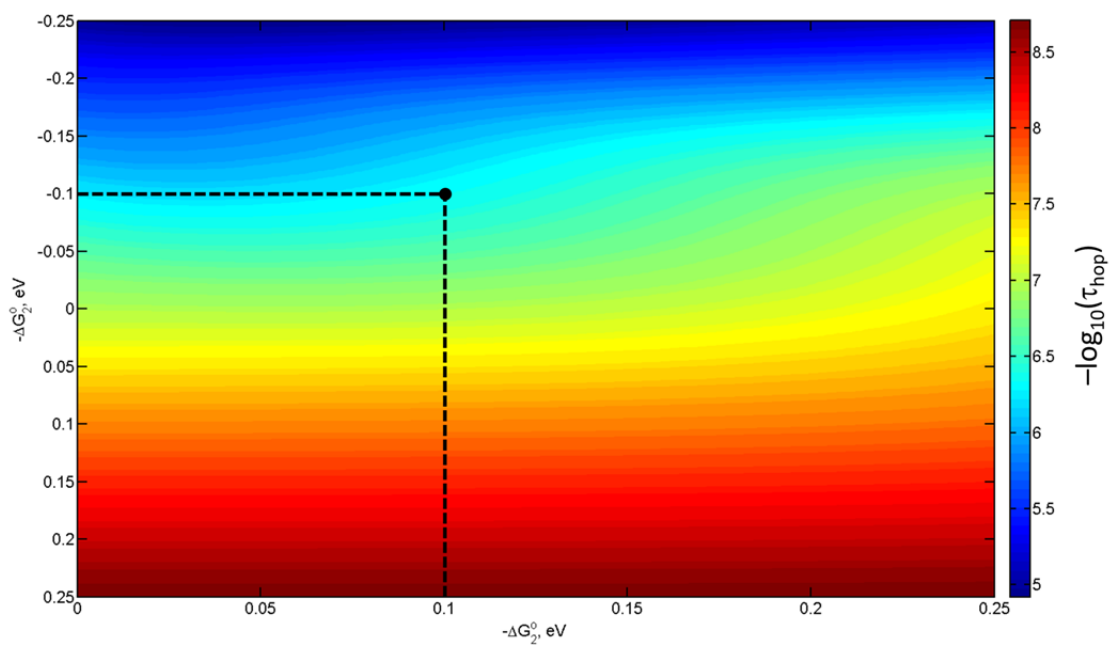
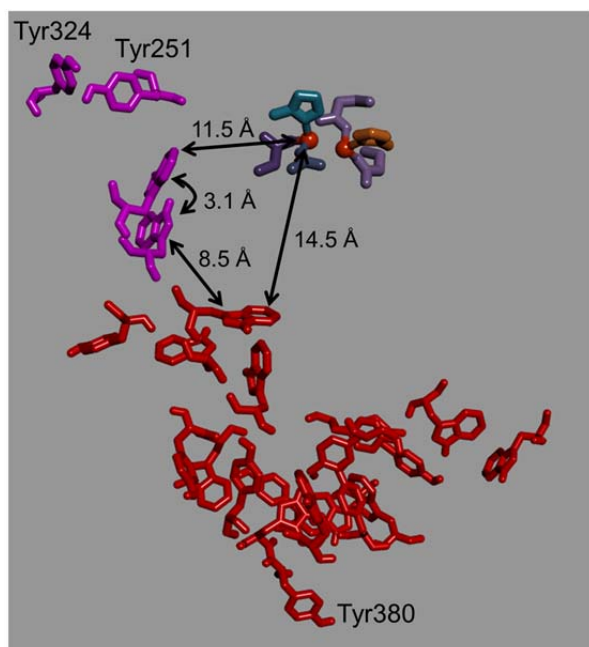


Fig. S6. Electron hopping map for Tyr/Trp chain in human KDM4A. Color indicates survival time (τ_{hop} , seconds) of a hole at the origin residue. Intersection of the dashed lines indicates location of estimated survival time point ($\sim 0.4 \mu\text{s}$).



Methane Monooxygenase
***Methylococcus capsulatus* (Bath)**
(PDB ID: 1MTY)

Fig. S7. Active site and Tyr/Trp chain residues in methane monooxygenase *Methylococcus capsulatus* (Bath).

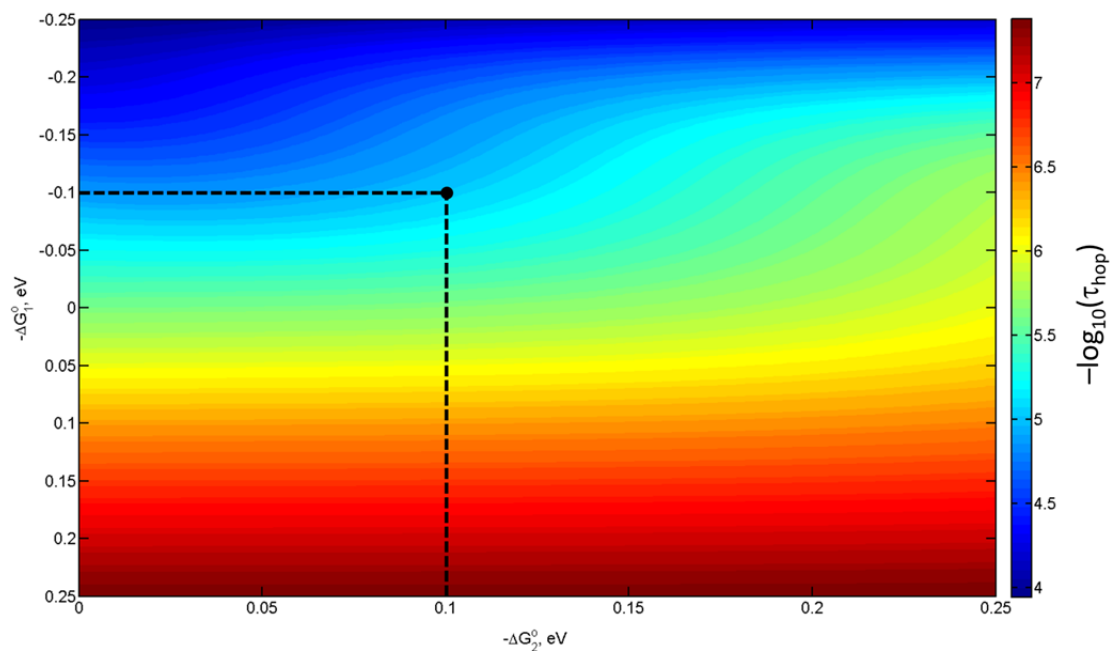


Fig. S8. Electron hopping map for Tyr/Trp chain in methane monooxygenase *Methylococcus capsulatus* (Bath). Color indicates survival time (τ_{hop} , seconds) of a hole at the origin residue. Intersection of the dashed lines indicates location of estimated survival time point ($\sim 9 \mu\text{s}$).