Identification of the Ah-receptor structural determinants for ligand preferences

Supplemental materials:

Figure S1

Figure S2

Figure S3

Figure S4

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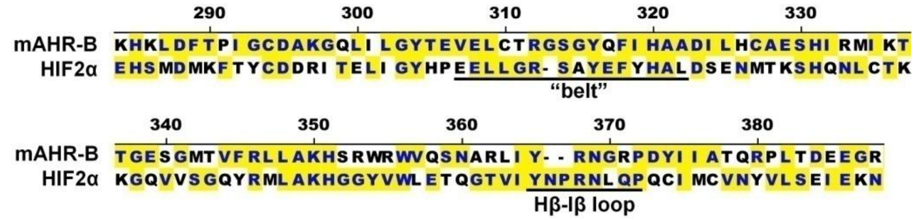


Figure S1. Sequence alignment of human HIF2α and the B allele of mouse AHR. The “belt” sequence and loop Hβ-Iβ are highlighted. Identical residues are highlighted in yellow.

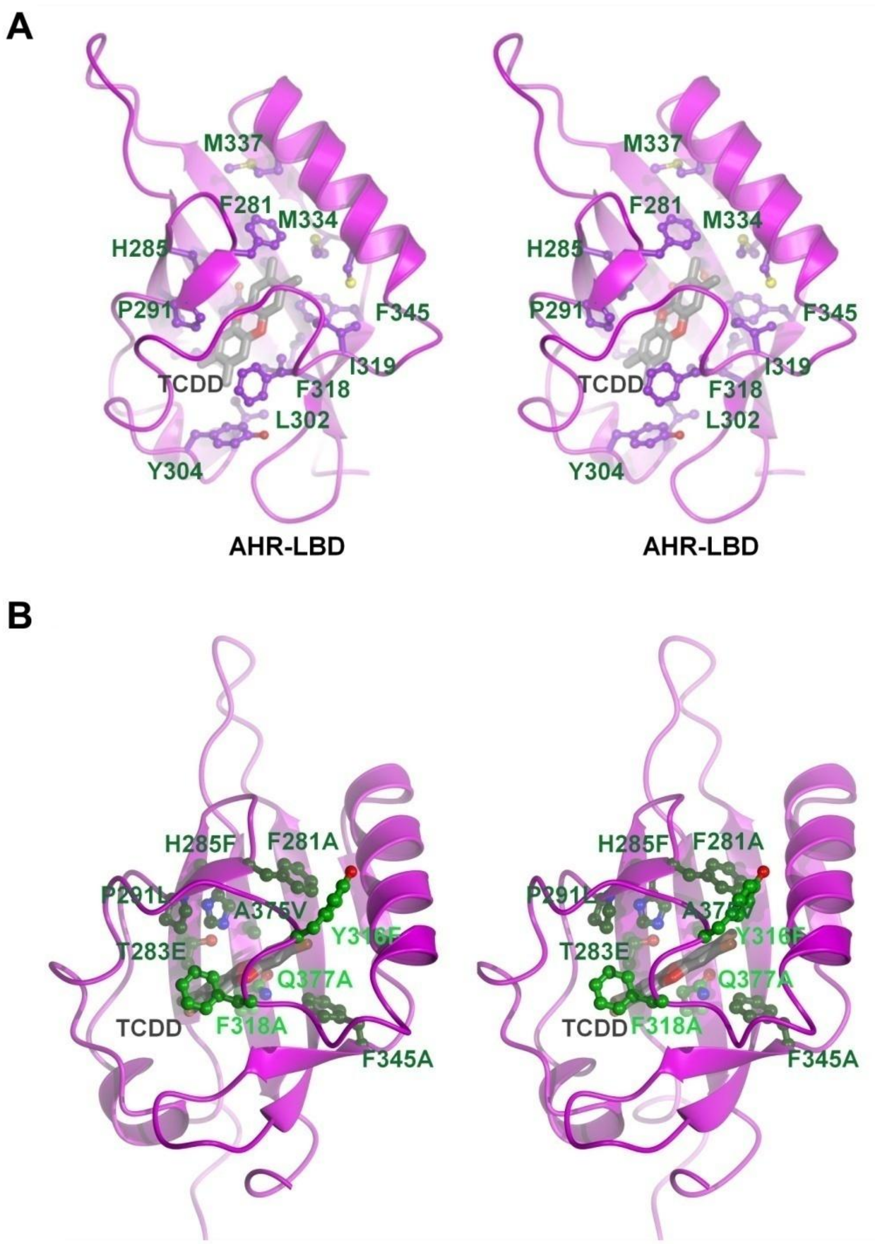
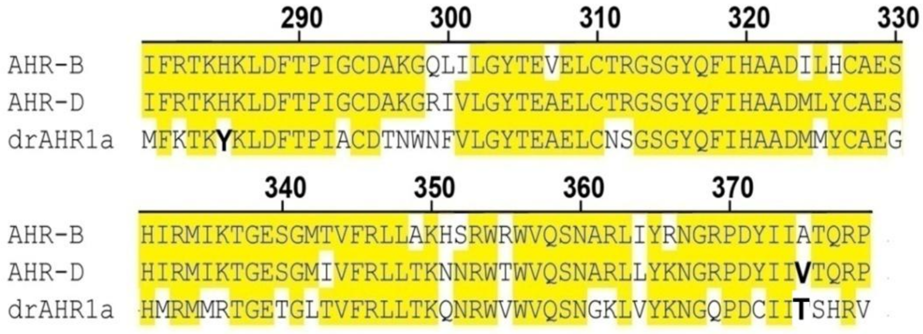

A
M337
F281
M334
H285
P291
F345
I319
TCDD
F318
L302
Y304
AHR-LBD
AHR-LBD
B
H285F
F281A
P291L
A375V
Y316F
T283E
Q377A
TCDD
F318A
F345A

Figure S2. The AHR residues lining the ligand binding pocket. (A) Stereo of the model of the mAHR-LBD bound to TCDD, illustrating residues lining the ligand binding pocket. These include F281, T283, H285, F289, P291, L302, Y304, F318, I319, C327, M334, M337, F345, L347, V357, S359, A375, Q377, and are selectively labeled. (B) Stereo of the model of the mAHR-LBD bound to TCDD, illustrating mutations shown in previous studies (29) that abolish (dark green) or compromise ligand binding (green).



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                    290       300       310       320       330
AHR-B     IFRTKHKLDFTPIGCDAKGQLILGYTEVELCTRGSGYQFIHAADILHCAES
AHR-D     IFRTKHKLDFTPIGCDAKGRIVLGYTEAELCTRGSGYQFIHAADMLYCAES
drAHR1a   MFKTKYKLDFTPIACDTNWNFVLGYTEAELCNSGSGYQFIHAADMMYCAEG

                   340       350       360       370
AHR-B     HIRMIKTGESGMTVFRLLAKHSRWRWVQSNARLIYRNGRPDYIIATQRP
AHR-D     HIRMIKTGESGMIVFRLLTKNNRWTWVQSNARLLYKNGRPDYIIVTQRP
drAHR1a   HMRMMRTGETGLTVFRLLTKQNRWVWVQSNGKLVYKNGQPDCIITSHRV
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Figure S3. Sequence alignment of mouse AHR B-allele, D-allele, and the nonfunctional allele of zebra fish (drAHR1a). Identical residues are highlighted in yellow. V375 in mouse D-allele and Y285/T375 in drAHR1a are highlighted in bold.

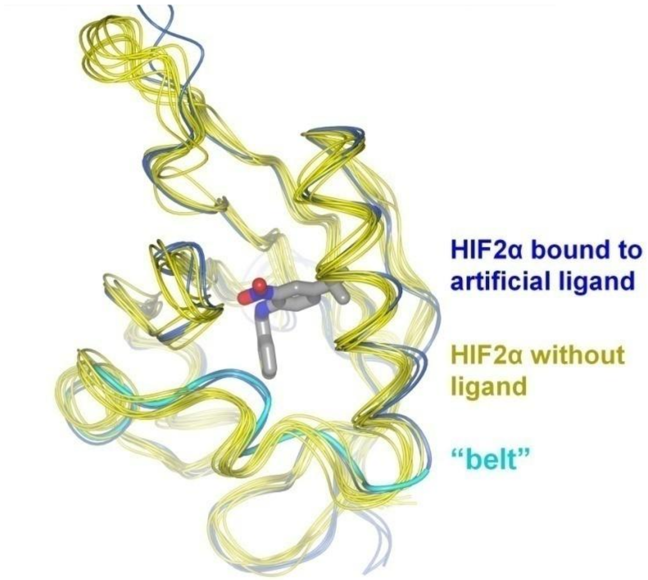

Figure S4. Alignment of crystal structures of HIF2α bound to artificial ligands (PDB codes: 3H7W, 3H82, 3F1N) (blue) and its NMR structures in the absence of ligands (PDB code: 2A24) (yellow). The “belt” in 3H7W is shown in cyan.