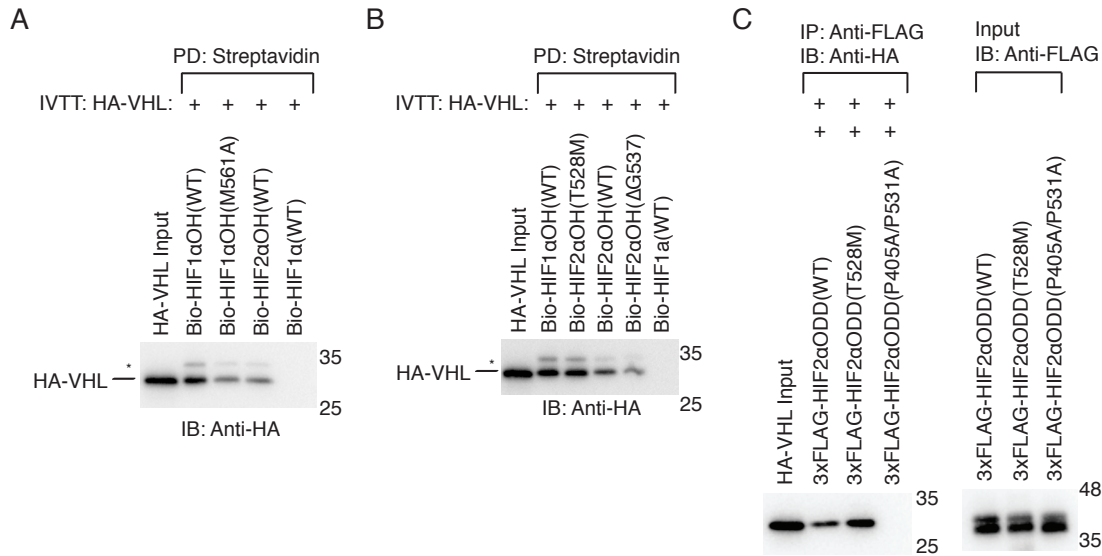


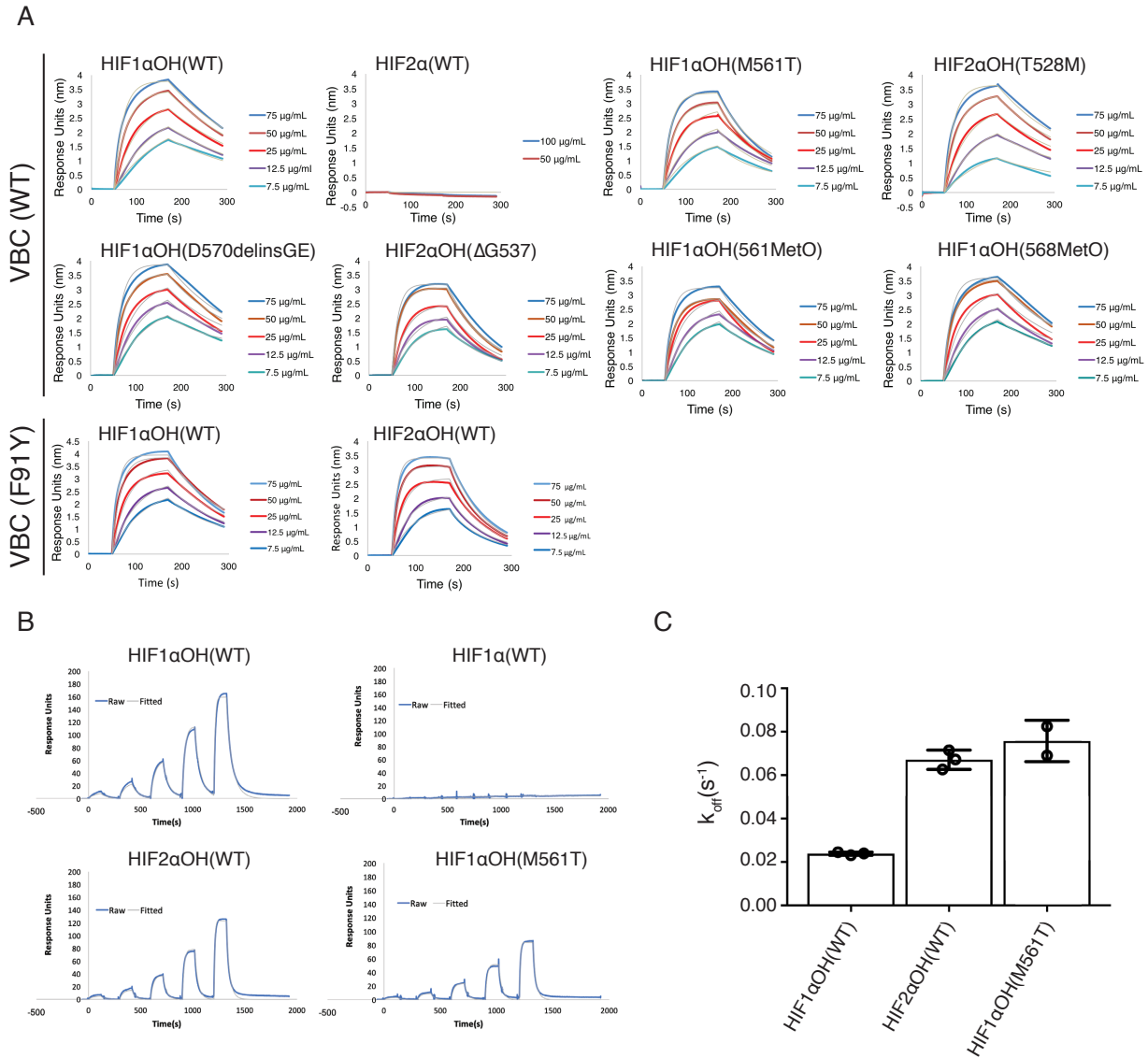
Evolution of metazoan oxygen-sensing involved a conserved divergence of VHL affinity for HIF1 α and HIF2 α

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Supplementary Information



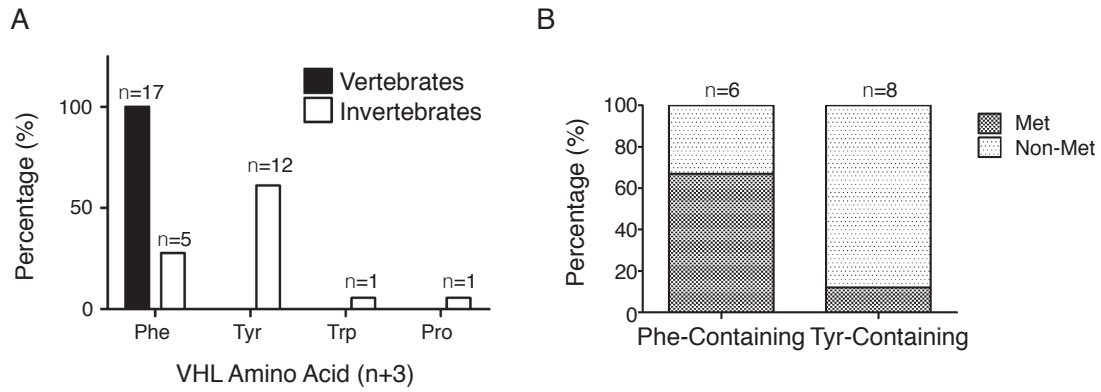
Supplementary Figure 1. Substitution of Met_{n-3} with alanine or threonine results in decreased affinity for pVHL. a, b Biotinylated HIFαOH peptides were immobilized on streptavidin- agarose beads and incubated with *in vitro* transcribed and translated (IVTT) pVHL. Streptavidin beads were pulled down (PD) and levels of HA-tagged pVHL were visualized via immunoblotting (IB). **c** 3xFLAG-HIF2α oxygen dependent degradation (ODD) domains were IVTT and incubated with purified HIS₆-PHD2 (181-426). Following hydroxylation (one hour), 3xFLAG-HIF2α ODD domain was immobilized on protein A beads coated with anti-FLAG antibody and incubated with IVTT HA-VHL. 3xFLAG-HIF2α ODD domain was immunoprecipitated (IP) and levels of HA-tagged VHL were visualized via immunoblotting (IB). Molecular weight markers (kDa) are labeled.



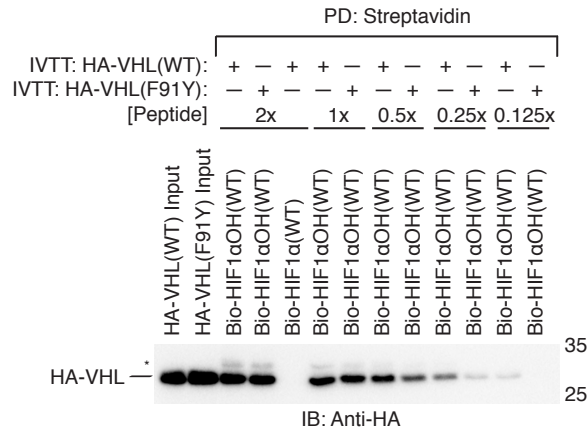
Supplementary Figure 2. Kinetic analysis of VHL complex binding to HIF α peptides. **a** Bi-layer interferometry kinetic analysis of pVHL-elongin B-elongin C (VBC), either WT or F91Y (where indicated), complex binding to biotinylated HIF α OH peptides. Biotinylated peptides were coupled to streptavidin-coated biosensors and monitored for binding to VBC complex at the indicated concentrations. The data were analyzed based on a 1:1 binding model using the BLItz Pro software with the fitted curves shown as gray lines. Sensorgrams are representative of three experiments conducted with independently purified proteins. **b, c** Surface plasmon resonance analysis of VBC(WT) complex binding to biotinylated HIF α OH peptides. Biotinylated peptides were coupled to a streptavidin-coated SPR chip. Single-cycle kinetics were carried out with increasing concentrations of VBC (0.123 μ g/mL, 0.37 μ g/mL, 1.11 μ g/mL, 3.33 μ g/mL, 10 μ g/mL) with a contact time of 120 seconds and a final dissociation step of 600 seconds. A flow rate of 30 μ L/min was maintained throughout the experiment. The data were analyzed based on a 1:1 binding model using the Biacore X100 evaluation software with the fitted curves shown as gray lines. **b** Representative sensorgrams. **c** The dissociation constants associated with VBC binding to HIF α peptides are shown on a linear scale. Values represent mean \pm s.d. Two technical replicates were performed for each peptide with an additional replication performed with independently purified protein for HIF1 α OH(WT) and HIF2 α OH(WT).

HIF1α	564	VHL	88	HIF2α	531
H. sapiens	DLDLEMLAPY	H. sapiens	VLPVWLNFDGE	H. sapiens	DLETLAPYIP
M. fascicularis	DLDLEMLAPY	I. tridecemlineatus	VLPVWLNFDGE	M. fascicularis	DLETLAPYIP
I. tridecemlineatus	DLDLEMLAPY	M. musculus	VLPVWLNFDGE	I. tridecemlineatus	DLETLAPYIP
M. musculus	DLDLEMLAPY	M. unguiculatus	VLPVWLNFDGE	M. musculus	DLETLAPYIP
M. unguiculatus	DLDLEMLAPY	C. hircus	VLPVWLNFDGE	M. unguiculatus	DLETLAPYIP
C. hircus	DLDLEMLAPY	D. leucas	VLPVWLNFDGE	C. hircus	DLETLAPYIP
D. leucas	DLDLEMLAPY	O. hannah	VSPVWLNFDGK	D. leucas	DLETLAPYIP
P. erythrurus	DLDLEMLAPY	P. vitticeps	VSPVWLNFDGK	P. erythrurus	DLETLAPYIP
P. przewalskii	DLDLEMLAPY	G. gallus	VLPVWLNFDGE	P. vitticeps	DLETLAPYIP
P. vitticeps	DLDLEMLAPY	C. caeruleus	VLPVWLNFDGE	G. gallus	DLETLAPYIP
O. hannah	DLDLEMLAPY	X. laevis	VQPVWLNFDGQ	A. Platyrrhynchos	DLETLAPYIP
G. gallus	DLDLEMLAPY	L. chalumnae	VQPVWLNFDGQ	C. livia	DLETLAPYIP
A. platyrrhynchos	DLDLEMLAPY	D. rerio	VKPVWLNFDGE	C. caeruleus	DLETLAPYIP
C. livia	DLDLEMLAPY	C. carpio	AEAWWLNFDAGK	L. lapponica	DLETLAPYIP
C. caeruleus	DLDLEMLAPY	O. tshawytscha	ARAWWLNFDGSH	X. laevis	DLETLAPYIP
L. lapponica_baueri	DLDLEMLAPY	R. typus	ARPWVWLNFDGV	X. tropicalis	DLETLAPYIP
X. laevis	DLDLEMLAPY	C. milii	VRPWVWLNFDGFF	L. chalumnae	DLETLAPYIP
R. temporaria	DLDLEMLAPY	P. marinus	ARPLWLNFDGQV	H. ocellatum	DLETLAPYIP
L. chalumnae	DLDLEMLAPY	S. kowalevskii	VDVWLNFDGQV	R. typus	DLETLAPYIP
F. annectens	GLDLEMLAPY	S. purpuratus	VDVWLNFDGQV	C. milii	DLETLAPYIP
H. ocellatum	NLDLEMLAPY	A. planci	VDIWLWLNFDGGE	D. rerio	DLETLAPYIP
R. typus	NLDLEMLAPY	C. gigas	ATLFWLNFDKGE	O. tshawytscha	DLETLAPYIP
M. canis	DLDLEMLAPY	C. virginica	ATLFWLNFDKGD	C. carpio	DLETLAPYIP
C. milii	GLDLEMLAPY	M. yessoensis	VDTVWLNFDGEA	P. marinus	DLETLAPYIP
A. gueldenstaedtii	DFDLEMLAPY	L. anatina	VDVWLNFDGEA	F. marinus	DLETLAPYIP
D. rerio	DLDLEMLAPY	I. scapularis	VDVWLNFDYNGT	S. kowalevskii	DLETLAPYIP
O. tshawytscha	DLDLEMLAPY	D. magna	VEVWLNFDYNGA	S. purpuratus	DLETLAPYIP
C. carpio	DLDLEMLAPY	O. pulex	VEVWLNFDYNGA	A. planci	DLETLAPYIP
P. marinus	DMLEMLAPY	O. abietinus	VGVWLNFDYQGH	C. gigas	DLDMDMRAPY
S. kowalevskii	TEELVMRAPY	N. vitripennis	TSVWLNFDYQSK	C. virginica	DLDMDMRAPY
S. purpuratus	CDELAMRAPY	T. cornetzi	ITLYWLNFDYQCG	M. yessoensis	EIDMDTRAPY
A. planci	. . DLSMRAPY	B. terrestris	VVLYWLNFDYQGR	L. anatina	EMEMYMRAPY
C. gigas	DLDMDMRAPY	C. elegans	VDVWLNFDYQSKQ	H. diversicolor	DVDLNMRRAPY
C. virginica	DLDMDMRAPY	O. faveolata	VKVLWLNFDYQGE	L. polyphemus	DEELFERAPY
M. yessoensis	EIDMDTRAPY	S. pistillata	VNLRWLNFDYSGE	D. magna	EELDRRAPY
L. anatina	EMEMYMRAPY	A. digitifera	VDVWLNFDYQGG	D. pulex	EELDRRAPY
H. diversicolor	DVDLNMRRAPY	E. pallida	VNLTWLNFDYNGR	N. lugens	ADDFAVTAPY
L. polyphemus	DEELFERAPY	T. adhaerens	AKMTLWLNFDYNGE	O. taurus	DPDLVMKAPY
D. magna	EELDRRAPY			O. abietinus	DDELALRAPY
D. pulex	EELDRRAPY			T. cornetzi	DEELALRAPY
N. lugens	ADDFAVTAPY			C. elegans	EPDLSCLAPF
O. taurus	DPDLVMKAPY			A. suum	NFDLQTLAPF
O. abietinus	DDELALRAPY			P. pacificus	DDSFDMNAPF
T. cornetzi	DEELALRAPY			E. pallida	DLDMDRDRAPF
C. elegans	EPDLSCLAPF			N. vectensis	SNELNRRAPY
A. suum	NFDLQTLAPF			O. faveolata	EENFDERAPF
P. pacificus	DDSFDMNAPF			S. pistillata	EENFDERAPF
E. pallida	DLDMDRDRAPF			T. adhaerens	KEEYDRLAPF
N. vectensis	SNELNRRAPY				
O. faveolata	EENFDERAPF				
S. pistillata	EENFDERAPF				
T. adhaerens	KEEYDRLAPF				

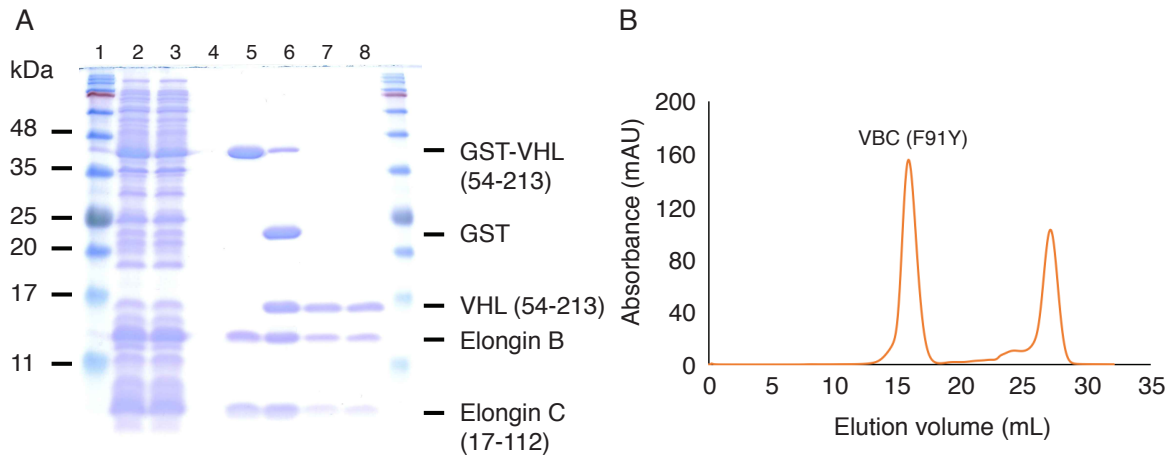
Supplementary Figure 3. Alignment of amino acid sequences. Annotated HIF1α, VHL, and HIF2α sequences were identified through use of BLASTP. Sequences were aligned using the MAFFT algorithm via the GUIDANCE webserver. Numbering of residues is based on the *H. sapiens* protein. Columns where >70% of residues are equivalent are colored in red and boxed in blue. Invariant residues are colored white on a red background. ESPrpt3 was used to display alignments.



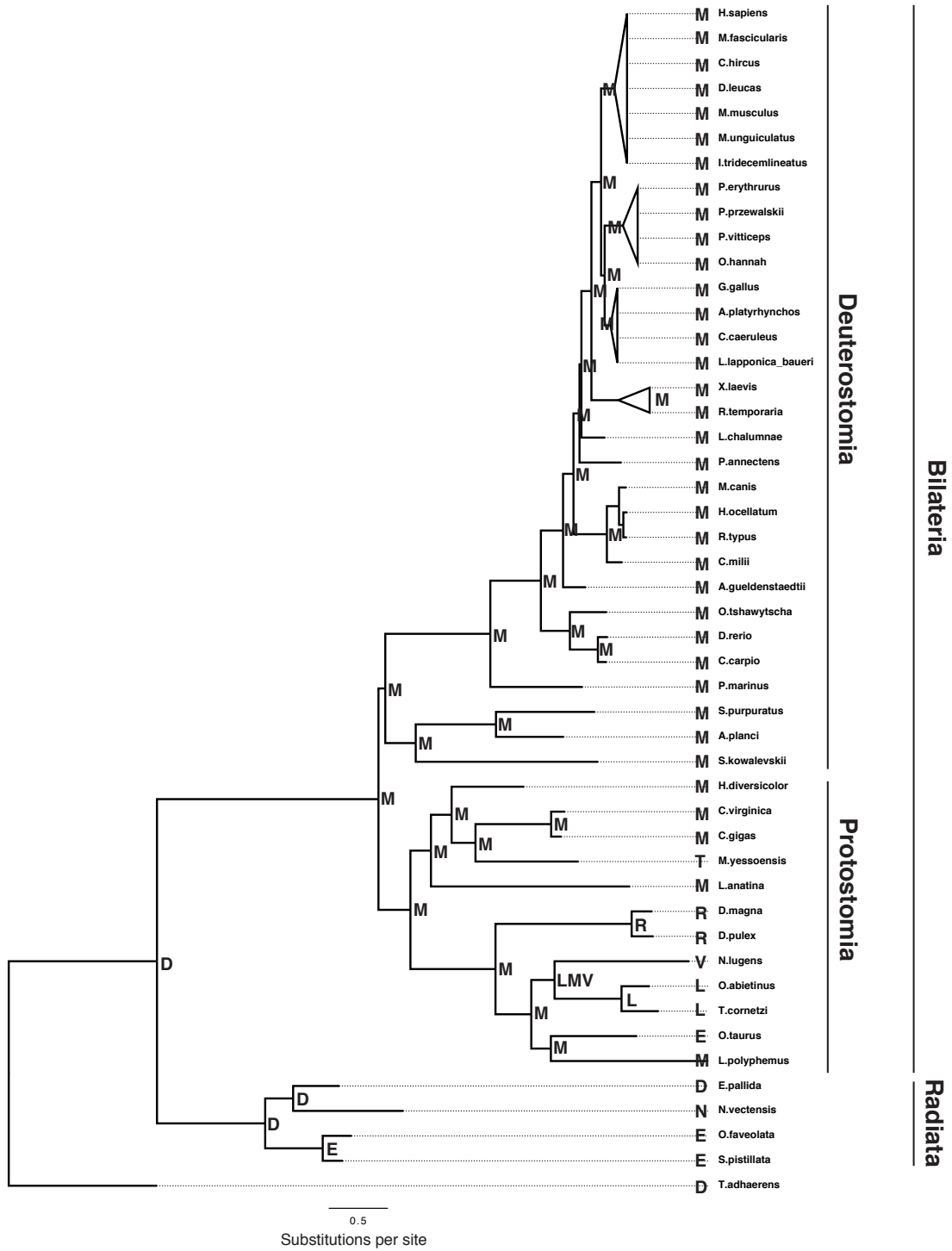
Supplementary Figure 4. VHL Phe_{n+3} is conserved in vertebrate species. **a** Annotated VHL sequences were identified through use of BLASTP. Sequences were aligned using the MAFFT algorithm via the GUIDANCE webserver. The frequency of the amino acid three residues C-terminal of an invariant tryptophan (VHL Trp88 in humans) is indicated for vertebrate and invertebrate species. **b** Based on VHL and HIF α sequence alignments, the frequency of VHL Phe_{n+3} and HIF α Met_{n-3} are indicated. As VHL Phe_{n+3} and HIF1 α Met_{n-3} are invariant in vertebrate species, the analysis is only conducted in invertebrate species for which an annotated VHL and HIF α sequences are available.



Supplementary Figure 5. Increased peptide concentration obscures differential binding of WT and F91Y VHL to HIF1αOH. 1x peptide concentration = 1.2 μg. Biotinylated HIFαOH peptides were immobilized on streptavidin-agarose beads and incubated with in vitro transcribed and translated (IVTT) pVHL. Streptavidin beads were pulled down (PD) and levels of HA-tagged pVHL were visualized via immunoblotting (IB). Molecular weight markers (kDa) are labeled.



Supplementary Figure 6. Purification of pVHL(F91Y)-elongin B-elongin C (VBC) complex. Transformed BL21(DE3) *E. coli* were induced to express GST-tagged pVHL₁₉ (residues 54-213) along with untagged elongin B and elongin C (17-112). (A) GST-VBC complex was affinity purified using glutathione sepharose resin. Thrombin was used to cleave the GST-tag from pVHL. Affinity purification was used to remove GST from the protein solution. SDS-PAGE analysis followed by Coomassie staining was employed to monitor successful cleavage of the GST-tag and purity of the sample. Lane 1 = protein ladder; lane 2 = input; lane 3 = flow-through; lane 4 = wash; lane 5 = elution; lane 6 = cleavage; lane 7 = affinity purification; lane 8 = 2 µg purified VBC following size exclusion chromatography (SEC). (B) VBC (F91Y) complex was purified to homogeneity using SEC. The VBC (F91Y) complex had an elution volume of approximately 16 mL. mAU = milli absorption units.



Supplementary Figure 7. Inference of ancestral HIF1 α sequence. Using a maximum parsimony method, the amino acid identity of HIF X_{n-3} was inferred at nodes during invertebrate evolution. The maximum likelihood phylogenetic tree (see Fig. 3a) was used as a guide. The set of states at each node is ordered from most likely to least likely, excluding states with probabilities below 5%.

Supplementary Table 1. List of Primers. Related to Experimental Procedures.

Primer Name	Primer Sequence (5'-3')
HIF1 α (387-581) FWD	ATTATTGAATTCTCAGGAACTGCTTTCTAATGGTGACAACTGATCGAAGG
HIF1 α (387-581) REV	ATTATTGCGGCCGCTCAGGAACTGCTTTCTAATGGTGACAACTGATCGAAGG
HIF2 α P405A FWD	TGGGGTGGCAGCCAGCTGGGCCA
HIF2 α P405A REV	TGGCCCAGCTGGCTGCCACCCCA
HIF2 α T528M FWD	GGGATATAGGGTGCCAGCATCTCCAAGTCCAGCTCA
HIF2 α T528M REV	TGAGCTGGACTTGGAGATGCTGGCACCCCTATATCCC
HIF1 α M561T FWD	GGGATATAGGGAGCTAACGTCTCCAAGTCTAAATCTG
HIF1 α M561T REV	CAGATTTAGACTTGGAGACGTTAGCTCCCTATATCCC
VHL F91Y FWD	TCGCCGTCGTAGTTGAGCCATACGGGC
VHL F91Y REV	GCCCGTATGGCTCAACTACGACGGCGA
VHL F91W FWD	GGCTCGCCGTCCCAGTTGAGCCATACGGG
VHL F91W REV	CCCGTATGGCTCAACTGGGACGGCGAGCC
VHL F91L FWD	GCTCGCCGTCTAAGTTGAGCCATACGGGC
VHL F91L REV	GCCCGTATGGCTCAACTTAGACGGCGAGC

Supplementary Table 2. Sequence ID for HIF1 α , HIF2 α , and VHL. Related to Experimental Procedures.

Species Name	Common Name	HIF1 Sequence ID	Gene ID	Protein ID
<i>Homo sapiens</i>	Human	HIF1 α Sequence ID	NM_001530.3	NP_001521.1
		HIF2 α Sequence ID	U81984.1	AAB41495
		VHL Sequence ID	NM_000551.3	NP_000542.1
<i>Macaca fascicularis</i>	Crab-eating macaque	HIF1 α Sequence ID	NM_001283896.1	NP_001270825.1
		HIF2 α Sequence ID	XM_005575965.2	XP_005576022.1
		VHL Sequence ID		
<i>Delphinapterus leucas</i>	Beluga whale	HIF1 α Sequence ID	KJ619999.1	AIB53793.1
		HIF2 α Sequence ID	KX227381.1	APX43029.1
		VHL Sequence ID	XM_022564705.1	XP_022420413.1
<i>Capra hircus</i>	Goat	HIF1 α Sequence ID	KC700026.1	AGM38929.1
		HIF2 α Sequence ID	XM_018055188.1	XP_017910677.1
		VHL Sequence ID	XM_018038280.1	XP_017893769.1
<i>Mus musculus</i>	Mouse	HIF1 α Sequence ID	AF003695.1	AAC53455.1
		HIF2 α Sequence ID	BC057870.1	AAH57870.1
		VHL Sequence ID	NM_009507.4	NP_033533.1
<i>Ictidomys tridecemlineatus</i>	Squirrel	HIF1 α Sequence ID	XM_013357468.2	XP_013212922.1
		HIF2 α Sequence ID	XM_005324504.3	XP_005324561.1
		VHL Sequence ID	XM_005343104.3	XP_005343161.2
<i>Meriones unguiculatus</i>	Gerbil	HIF1 α Sequence ID	XM_021651031.1	XP_021506706.1
		HIF2 α Sequence ID	XM_021643571.1	XP_021499246.1
		VHL Sequence ID	XM_021637655.1	XP_021493330.1
<i>Gallus gallus</i>	Chicken	HIF1 α Sequence ID	NM_204297.1	NP_989628.1
		HIF2 α Sequence ID	NM_204807.2	NP_990138.1
		VHL Sequence ID	XM_414447.5	XP_414447.3
<i>Anas platyrhynchos</i>	Mallard	HIF1 α Sequence ID	XM_005029943.3	XP_005030000.2
		HIF2 α Sequence ID	XM_005009804.3	XP_005009861.2
		VHL Sequence ID		
<i>Limosa lapponica baueri</i>	Bar-tailed godwit	HIF1 α Sequence ID	KZ506160.1	PKU41137.1
		HIF2 α Sequence ID	KZ505646.1	PKU48810.1
		VHL Sequence ID		
<i>Cyanistes caeruleus</i>	Blue tit	HIF1 α Sequence ID	XM_023927146.1	XP_023782914.1
		HIF2 α Sequence ID	XM_023924504.1	XP_023780272.1
		VHL Sequence ID	XM_023935659.1	XP_023791427.1
<i>Columba livia</i>	Rock pigeon	HIF1 α Sequence ID	AKCR02000005.1	PKK31254.1
		HIF2 α Sequence ID	AKCR02000024.1	PKK26737
		VHL Sequence ID		
<i>Phrynocephalus przewalskii</i>	Toadhead Agama	HIF1 α Sequence ID	KP696482.1	ALS35220.1
		HIF2 α Sequence ID		
		VHL Sequence ID		
<i>Phrynocephalus erythrurus</i>	Agama	HIF1 α Sequence ID	KP696483.1	ALS35221.1
		HIF2 α Sequence ID	KP696480.1	ALS35218.1
		VHL Sequence ID		
<i>Pogona vitticeps</i>	Central bearded dragon	HIF1 α Sequence ID	XM_020813439.1	XP_020669098.1
		HIF2 α Sequence ID	XM_020796898.1	XP_020652557.1
		VHL Sequence ID	XM_020791430.1	XP_020647089.1
<i>Ophiophagus hannah</i>	King cobra	HIF1 α Sequence ID	AZIM01002394.1	ETE64108.1
		HIF2 α Sequence ID		
		VHL Sequence ID	AZIM01000385.1	ETE71348.1
<i>Xenopus laevis</i>		HIF1 α Sequence ID	DQ529235.1	ABF71072.1

	African clawed frog	HIF2 α Sequence ID	NM_001092249.1	NP_001085718.1
		VHL Sequence ID	KC700047.1	AHE80969.1
<i>Xenopus tropicalis</i>	Western clawed frog	HIF1 α Sequence ID		
		HIF2 α Sequence ID	NM_001005647.1	NP_001005647.1
		VHL Sequence ID		
<i>Rana temporaria</i>	Common frog	HIF1 α Sequence ID	EU262663.1	ABY86629.1
		HIF2 α Sequence ID		
		VHL Sequence ID		
<i>Protopterus annectens</i>	West African lungfish	HIF1 α Sequence ID	JQ031040.1	AFU07559.1
		HIF2 α Sequence ID		
		VHL Sequence ID		
<i>Latimeria chalumnae</i>	Coelacanth	HIF1 α Sequence ID	XM_005986412.2	XP_005986474.1
		HIF2 α Sequence ID	XM_006007491.2	XP_006007553.1
		VHL Sequence ID	XM_005987945.2	XP_005988007.1
<i>Danio rerio</i>	Zebrafish	HIF1 α Sequence ID	NM_001310042.1	NP_001296971.1
		HIF2 α Sequence ID	NM_001039806.2	NP_001034895.2
		VHL Sequence ID	NM_001080684.1	NP_001074153.1
<i>Oncorhynchus tshawytscha</i>	Chinook Salmon	HIF1 α Sequence ID	XM_024437278.1	XP_024293046.1
		HIF2 α Sequence ID	XM_024388216.1	XP_024243984.1
		VHL Sequence ID	XM_024407786.1	XP_024263554.1
<i>Cyprinus carpio</i>	Common carp	HIF1 α Sequence ID	EU144225.1	ABV59209.1
		HIF2 α Sequence ID	XM_019113102.1	XP_018968647.1
		VHL Sequence ID	XM_019077133.1	XP_018932678.1
<i>Acipenser gueldenstaedtii</i>	Russian sturgeon	HIF1 α Sequence ID	EF100701.1	ABO26712.1
		HIF2 α Sequence ID		
		VHL Sequence ID		
<i>Mustelus canis</i>	Smooth dogfish	HIF1 α Sequence ID	EU262662.1	ABY86628.1
		HIF2 α Sequence ID		
		VHL Sequence ID		
<i>Hemiscyllium ocellatum</i>	Epaulette shark	HIF1 α Sequence ID	EU262661.1	ABY86627.1
		HIF2 α Sequence ID	GQ152300.1	ADD59897.1
		VHL Sequence ID		
<i>Rhincodon typus</i>	Whale shark	HIF1 α Sequence ID	XM_020515091.1	XP_020370680.1
		HIF2 α Sequence ID	XM_020510059.1	XP_020365648.1
		VHL Sequence ID	XM_020532548.1	XP_020388137.1
<i>Callorhynchus milii</i>	Elephant shark	HIF1 α Sequence ID	XM_007903838.1	XP_007902029.1
		HIF2 α Sequence ID	XM_007896863.1	XP_007895054.1
		VHL Sequence ID	XM_007904937.1	XP_007903128.1
<i>Petromyzon marinus</i>	Lamprey	HIF1 α Sequence ID	ENSPMAG00000000126	ENSPMAT00000000148.1
		HIF2 α Sequence ID	ENSPMAG000000009272	ENSPMAT00000010244.1
		VHL Sequence ID	ENSPMAG000000009828.1	ENSPMAP00000010802.1
<i>Saccoglossus kowalevskii</i>	Acorn worm	HIF1 α Sequence ID	XM_002733741.3	XP_002733787.2
		HIF2 α Sequence ID		
		VHL Sequence ID	XM_002733273.2	XP_002733319.1
<i>Strongylocentrotus purpuratus</i>	Pacific purple sea urchin	HIF1 α Sequence ID	KX786251.1	ASL69982.1
		VHL Sequence ID	KX786255.1	ASL69986.1
<i>Acanthaster planci</i>	Crown-of-thorns starfish	HIF1 α Sequence ID	XM_022242264.1	XP_022097956.1
		VHL Sequence ID	XM_022236676.1	XP_022092368.1
<i>Haliotis diversicolor</i>	Sea snail	HIF1 α Sequence ID	KC149963.1	AGE97172.1
		VHL Sequence ID		
<i>Crassostrea gigas</i>	Pacific oyster	HIF1 α Sequence ID	NM_001305337.1	NP_001292266.1
		VHL Sequence ID	XM_011431794.2	XP_011430096.1

<i>Crassostrea virginica</i>	Eastern oyster	HIF1 α Sequence ID	HM441076.1	AED87588.1
		VHL Sequence ID	XM_022484237.1	XP_022339945.1
<i>Mizuhopecten yessoensis</i>	Yesso scallop	HIF1 α Sequence ID	XM_021497943.1	XP_021353618.1
		VHL Sequence ID	XM_021485147.1	XP_021340822.1
<i>Lingula anatina</i>	Lamp shell	HIF1 α Sequence ID	XM_013531134.2	XP_013386588.1
		VHL Sequence ID	XM_013557922.1	XP_013413376.1
<i>Orussus abietinus</i>	Parasitic wood wasp	HIF1 α Sequence ID	XM_012420115.2	XP_012275538.1
		VHL Sequence ID	XM_012420856.1	XP_012276279.1
<i>Nasonia vitripennis</i>	Jewel wasp	HIF1 α Sequence ID		
		VHL Sequence ID	XM_016983273.1	XP_016838762.1
<i>Bombus terrestris</i>	Buff-tailed bumblebee	HIF1 α Sequence ID		
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<i>Trachymyrmex cornetzi</i>	Ant	HIF1 α Sequence ID	KQ978957.1	KYN27213.1
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<i>Nilaparvata lugens</i>	Brown planthopper	HIF1 α Sequence ID	XM_022331880.1	XP_022187572.1
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<i>Daphnia pulex</i>	Waterflea	HIF1 α Sequence ID	GL732533.1	EFX84860.1
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<i>Caenorhabditis elegans</i>	Roundworm	HIF1 α Sequence ID	NM_075607.5	NP_508008.4
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<i>Ascaris suum</i>	Pig roundworm	HIF1 α Sequence ID	AB520828.1	BAJ17131.1
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<i>Pristionchus pacificus</i>	Roundworm	HIF1 α Sequence ID	ABKE03000053.1	PDM75007.1
		VHL Sequence ID		
<i>Exaiptasia pallida</i>	sea anemone	HIF1 α Sequence ID	LJWW01000106.1	KXJ20783.1
		VHL Sequence ID	XM_021061147.1	XP_020916806.1
<i>Nematostella vectensis</i>	Starlet sea anemone	HIF1 α Sequence ID	KJ411881.1	AII22158.1
		VHL Sequence ID		
<i>Orbicella faveolata</i>	mountainous star coral	HIF1 α Sequence ID	XM_020774709.1	XP_020630368.1
		VHL Sequence ID	XM_020746540.1	XP_020602199.1
<i>Stylophora pistillata</i>	Smooth cauliflower coral	HIF1 α Sequence ID	XM_022941810.1	XP_022797545.1
		VHL Sequence ID	XM_022948633.1	XP_022804368.1
<i>Acropora digitifera</i>	Coral	HIF1 α Sequence ID		
		VHL Sequence ID	XM_015898670.1	XP_015754156.1
<i>Trichoplax adhaerens</i>	Tablet animal	HIF1 α Sequence ID	JQ844128.1	AFM37575.1
		VHL Sequence ID		Triad1P7508