Figure S1

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Gene	NF-κB	HIF	Function
COX2	**X**	**X**	**Prostanoid synthesis**
CXCR4	**X**	**X**	**Chemokine receptor**
MMP9	**X**	**X**	**Matrix remodeling enzyme**
SERPINE1 (PAI-1)	**X**	**X**	**Fibrinolytic system**
SNAI1 (Snail1)	**X**	**X**	**EMT**
TWIST1	**X**	**X**	**EMT**
ZEB1	**X**	**X**	**EMT**
ZEB2	**X**	**X**	**EMT**
LOX		**X**	**Matrix remodeling enzyme**
MET		**X**	**Growth factor receptor**

Figure S1: Table summarizing the function and regulation of a selected panel of genes investigated in Figure 3.

Figure S2

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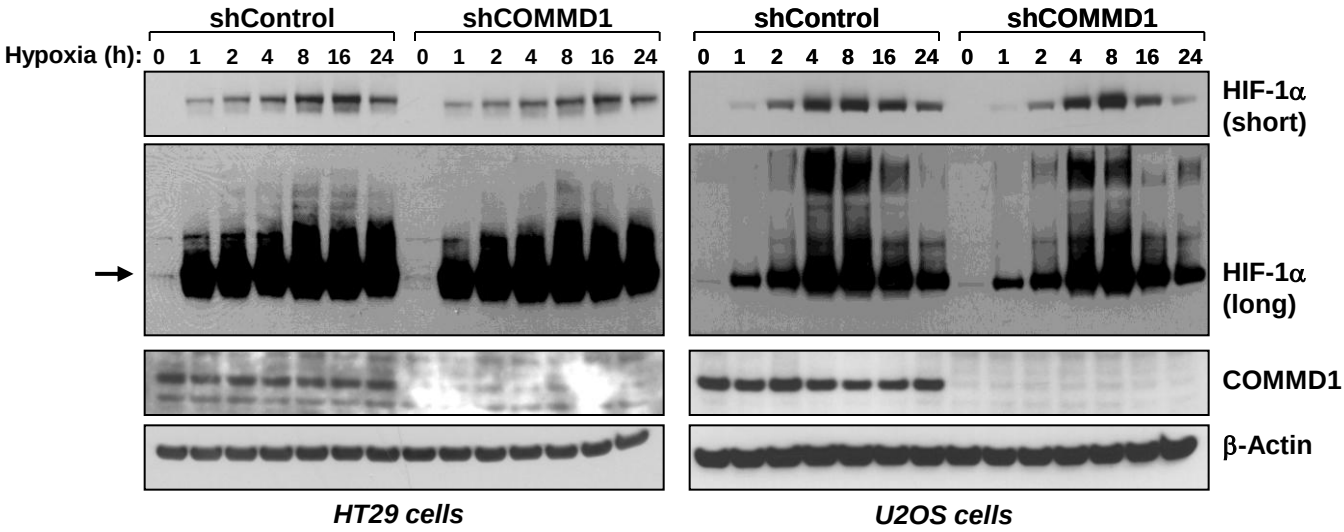

Figure S2: Time course accumulation of HIF-1α and the effect of COMMD1 deficiency. The indicated cell lines were placed in a 3% oxygen incubator. After growth under hypoxia for the indicated amounts of time, the cells were promptly lyzed and the material was analyzed by western blot as shown. A long exposure of the HIF-1α blot is shown to demonstrate detectable expression under normoxia (arrow).

Figure S3

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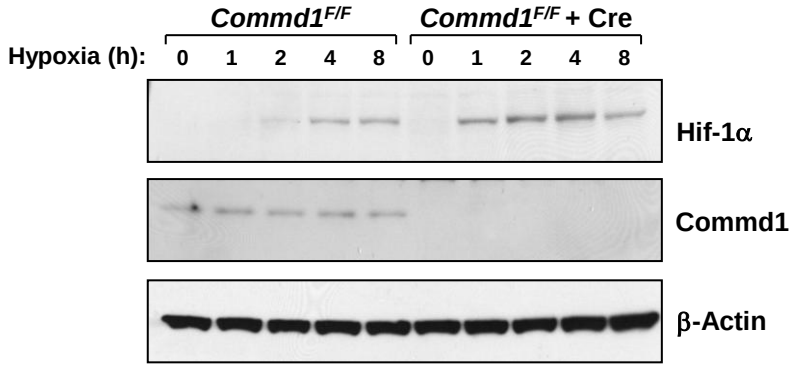

Figure S3: Hif-1α is stabilized in Commd1 deficient mouse embryo fibroblast (MEFs). MEFs were obtained from E14 embryos carrying LoxP sites around the first exon of Commd1 (*Commd1$^{F/F}$*). The cells were immortalized in culture by lentiviral infection to stably express E1A and Ras. These cultures were subsequently infected transiently with adenoviruses expressing the Cre recombinase (*Commd1$^{F/F}$* + Cre) or an adenovirus control expressing LacZ (*Commd1$^{F/F}$*). Loss of Commd1 expression after Cre expression was confirmed by western blot. Thereafter, the indicated cell lines were placed in a 3% oxygen incubator. After growth under hypoxia for the indicated amounts of time, the cells were promptly lyzed and the material was analyzed by western blot as shown.

Figure S4

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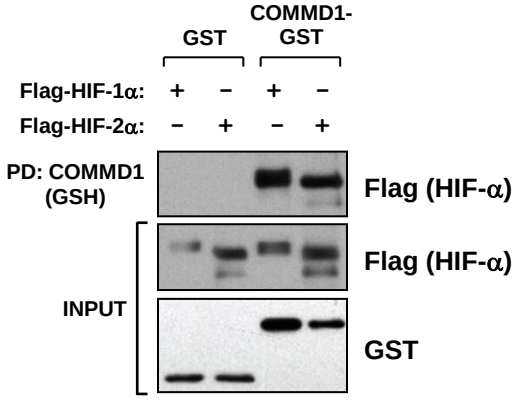

Figure S4: Coprecipitation between HIF-2α and COMMD1. HEK293 cells were cotransfected to express COMMD1-GST (or GST as a control) along with HIF-1α or HIF-2α. Upon harvesting of cellular lysates, COMMD1-GST was precipitated and the presence of either HIF-α subunit was determined by immunoblotting.

Figure S5

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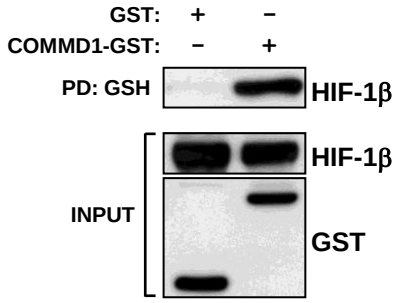

Figure S5: Coprecipitation between HIF-1β and COMMD1. HEK293 cells were cotransfected to express COMMD1-GST (or GST as a control) along with HIF-1β. Upon harvesting of cellular lysates, COMMD1-GST was precipitated and the presence of HIF-1β was determined by immunoblotting.

Figure S6

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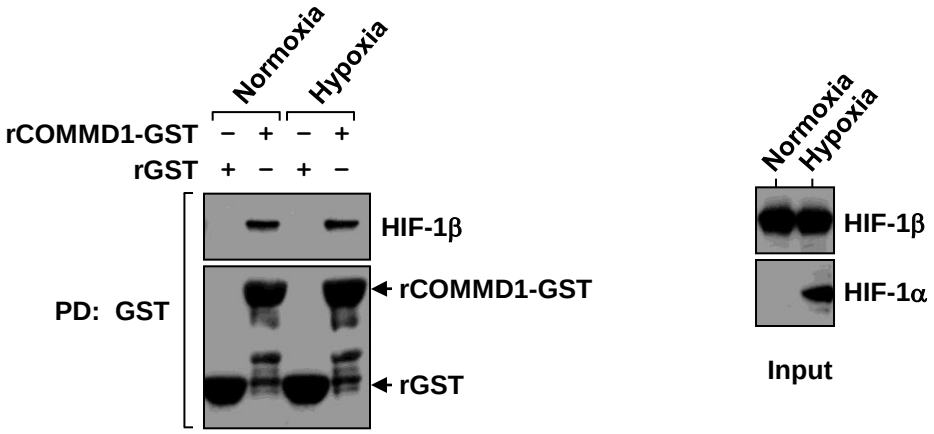

Figure S6: *In vitro* binding between HIF-1β and COMMD1. Lysates were obtained HEK293 cells under normoxic or hypoxic conditions (3% oxygen for 6 hours). The accumulation of HIF-1α was demonstrated in the input material immunoblotted for either HIF-1β or -1α (right panel). These lysates were mixed with recombinant COMMD1-GST or GST proteins prepared in *E. coli*. After a 3 hour incubation at 4 C, the recombinant proteins were precipitated from the lysate and the presence of bound endogenous HIF-1β was determined by immunoblotting.

Figure S7

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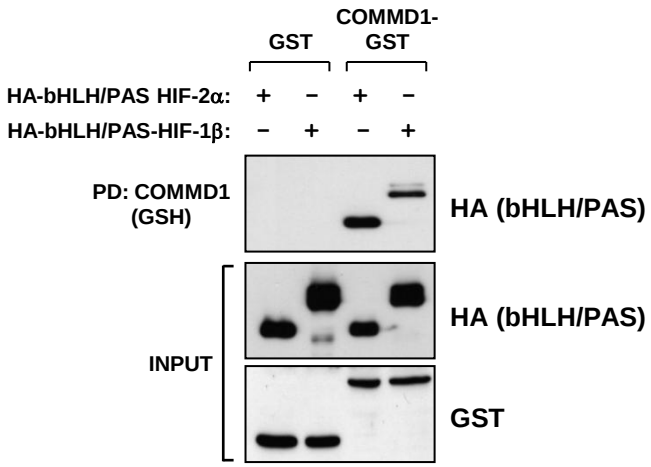

Figure S7: COMMD1 binds to the bHLH/PAS domains of HIF-2α and HIF-1β. HEK293 cells were cotransfected to express COMMD1-GST (or GST as a control) along with the indicated bHLH/PAS domains of HIF-2α or HIF-1β. Upon harvesting of cellular lysates, COMMD1-GST was precipitated and the presence of associated bHLH/PAS truncated proteins was determined by immunoblotting.