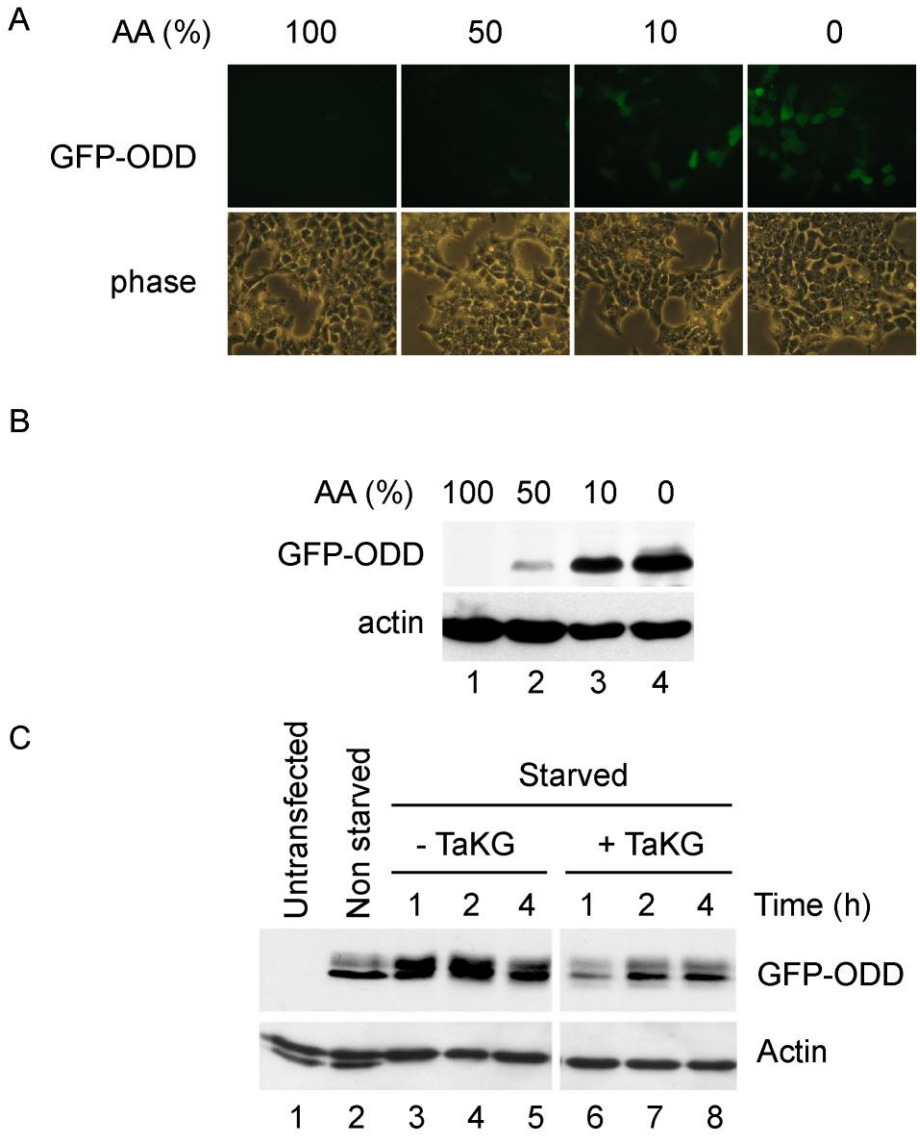
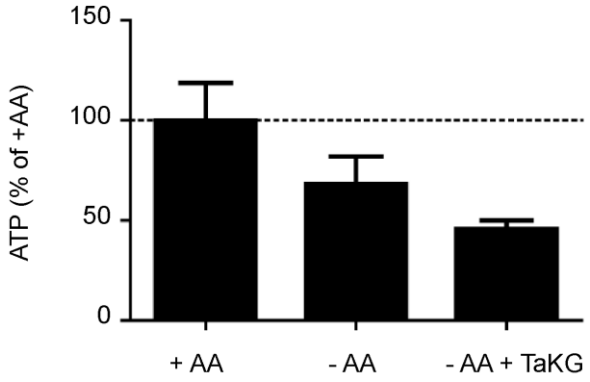
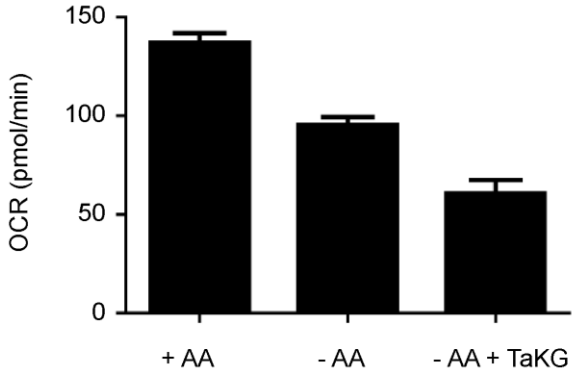


Supplementary Figure S1. (**A**, **B**) GFP-ODD accumulation examined microscopically (A) or by western blot (B) in HCT116 cells upon dose-dependent withdrawal of amino acids. (**C**) U2OS cells were transiently transfected with GFP-ODD and 48 hours later incubated under starving conditions for 4 hours. Then, cells were treated with either vehicle or TaKG for the indicated time. Accumulation of GFP-ODD was analyzed by western blot.

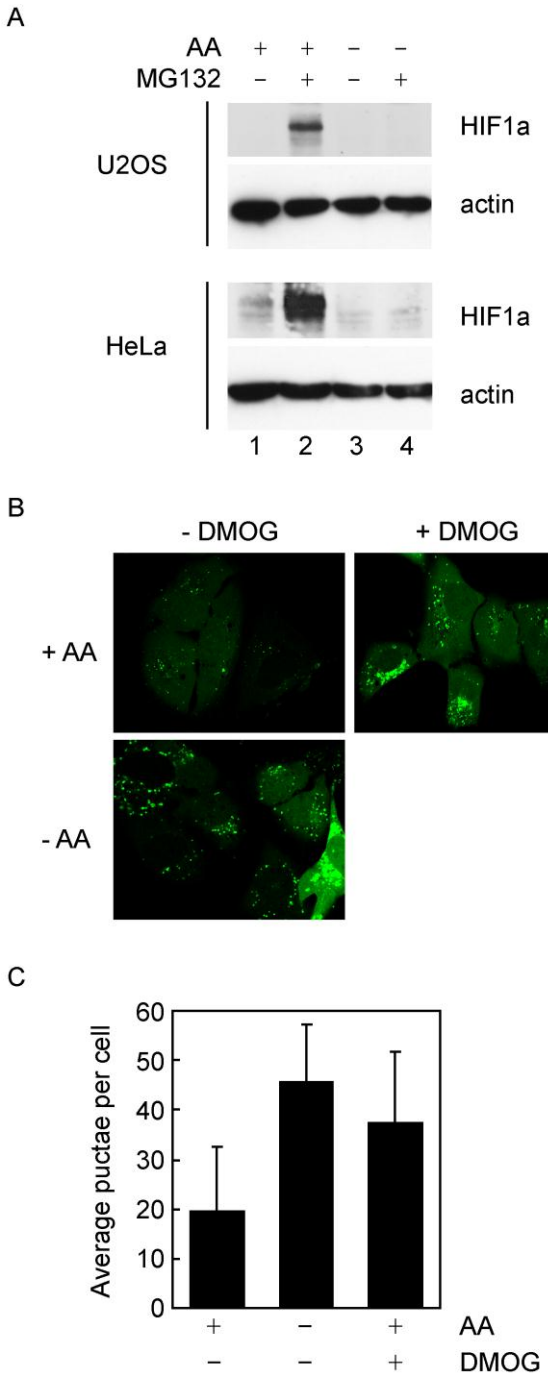
A



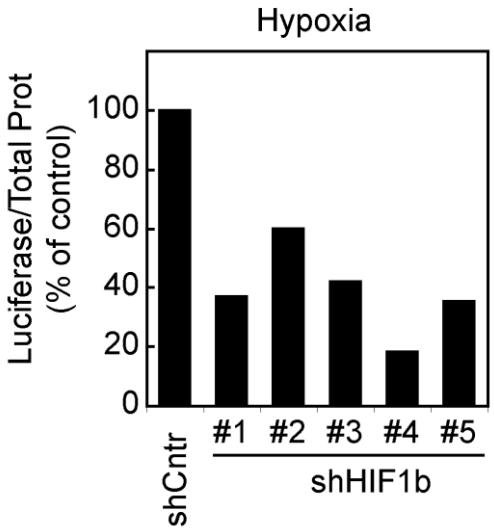
B



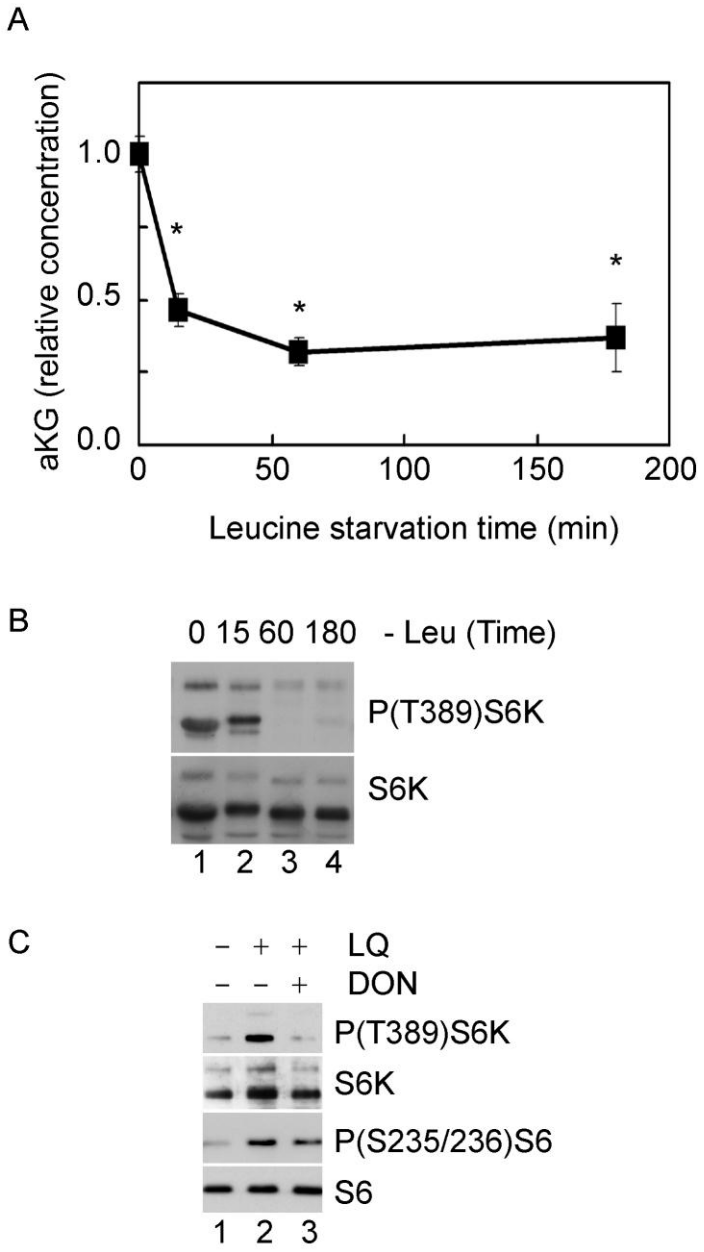
Supplementary Figure S2. Levels of ATP (**A**) and oxygen consumption (**B**) in fed, starved and TaKG re-stimulated U2OS cells



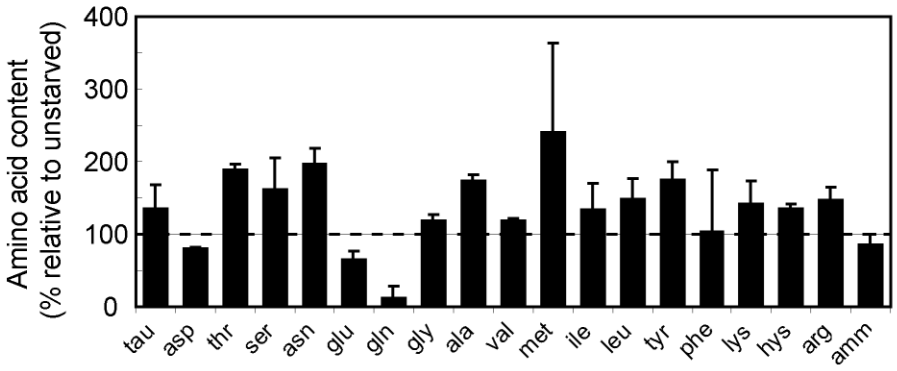
Supplementary Figure S3. (**A**) HIF1α accumulation upon MG132 treatment in U2OS and HeLa cells incubated either in the presence or the absence of amino acids for 2 hours (**B**, **C**) U2OS cells stably expressing GFP-LC3 were incubated for 5 hours either in the presence or absence of amino acids with or without DMOG as indicated. Aggregation of GFP-LC3 was analyzed by fluorescence microscopy (B) and quantified (C).



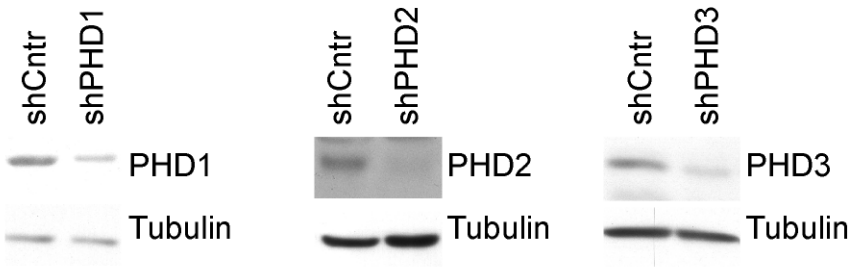
Supplementary Figure S4. U2OS were co-transfected with wild type pGL2/HRE-luciferase and with 5 different shRNA plasmids against HIF1β/ARNT. 48 hours later cells were incubated for 12 hour in hypoxia and luciferase intensity was measured. Clone #4 gave the higher decrease in luciferase levels and was therefore selected for further assays.



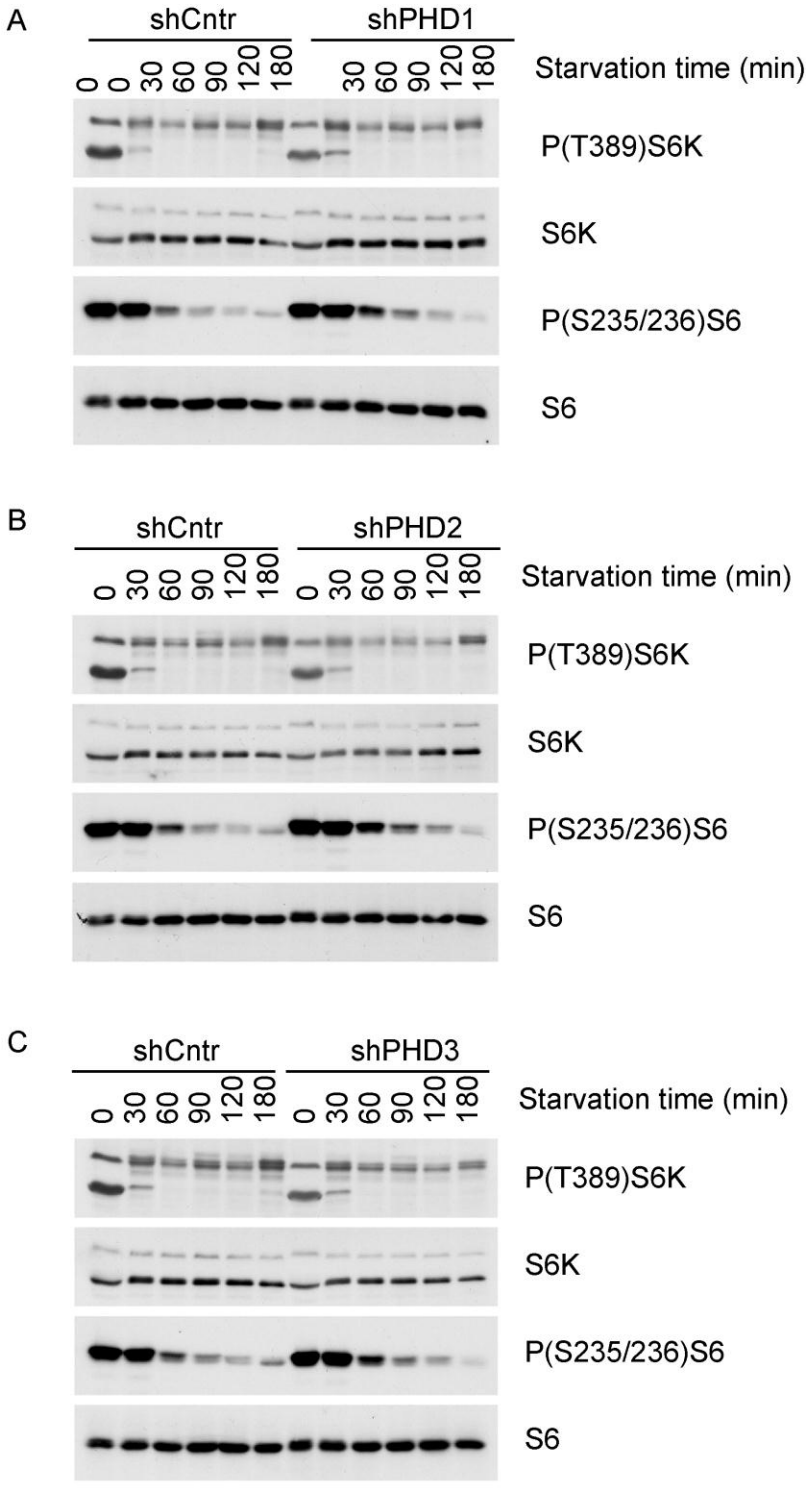
Supplementary Figure S5. (**A**) Intracellular aKG in U2OS cells was measured at different time points after leucine withdrawal. Levels were relative to those obtained prior to amino acid removal. Results represent the average and standard deviation of three independent experiments (*, $p<0.05$). (**B**) S6K phosphorylation was measured by western blot at different time points after leucine withdrawal. (**C**) U2OS cells were starved for all amino acids for 2 hours and then re-stimulated with leucine and glutamine (LQ) either in the presence or the absence of DON as indicated.



Supplementary Figure S6. Intracellular amino acid content level of U2OS after 1 hour of glutamine starvation (values are referred as percentage of change for each amino acid respect to non-starved cells).



Supplementary Figure S7. U2OS cells were transfected with shRNA plasmids for PHD1, PHD2 or PHD3. 48 hours later PHD levels were analyzed by western blot.



Supplementary Figure S8. U2OS cells were transiently transfected with a plasmid containing either scrambled shRNA (shSRC), or shRNA against PHD1 (**A**), PHD2 (**B**) or PHD3 (**C**). After 48 hours, transfected cells were starved for amino acids at different times as indicated and the phosphorylation state of S6K and S6 was quantified by western blot.