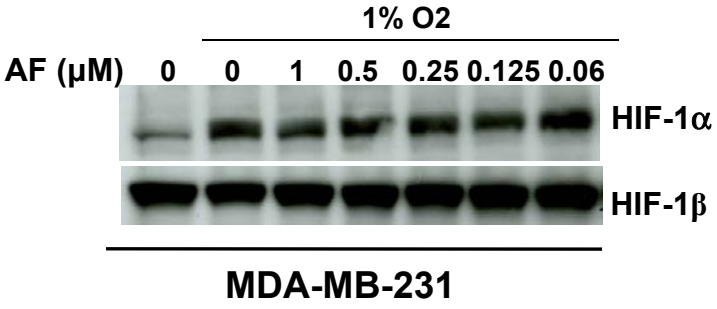
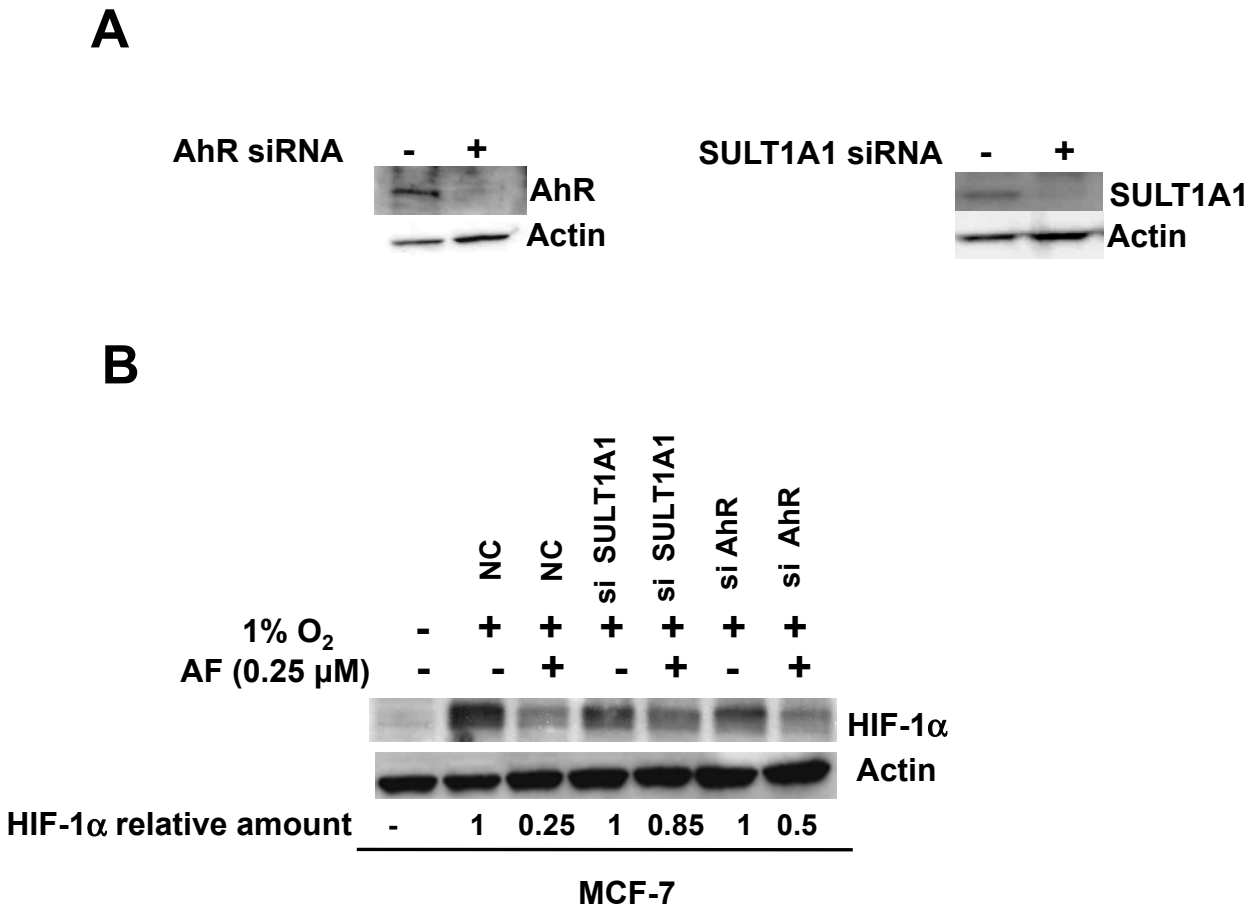
# Supplementary Figure 1



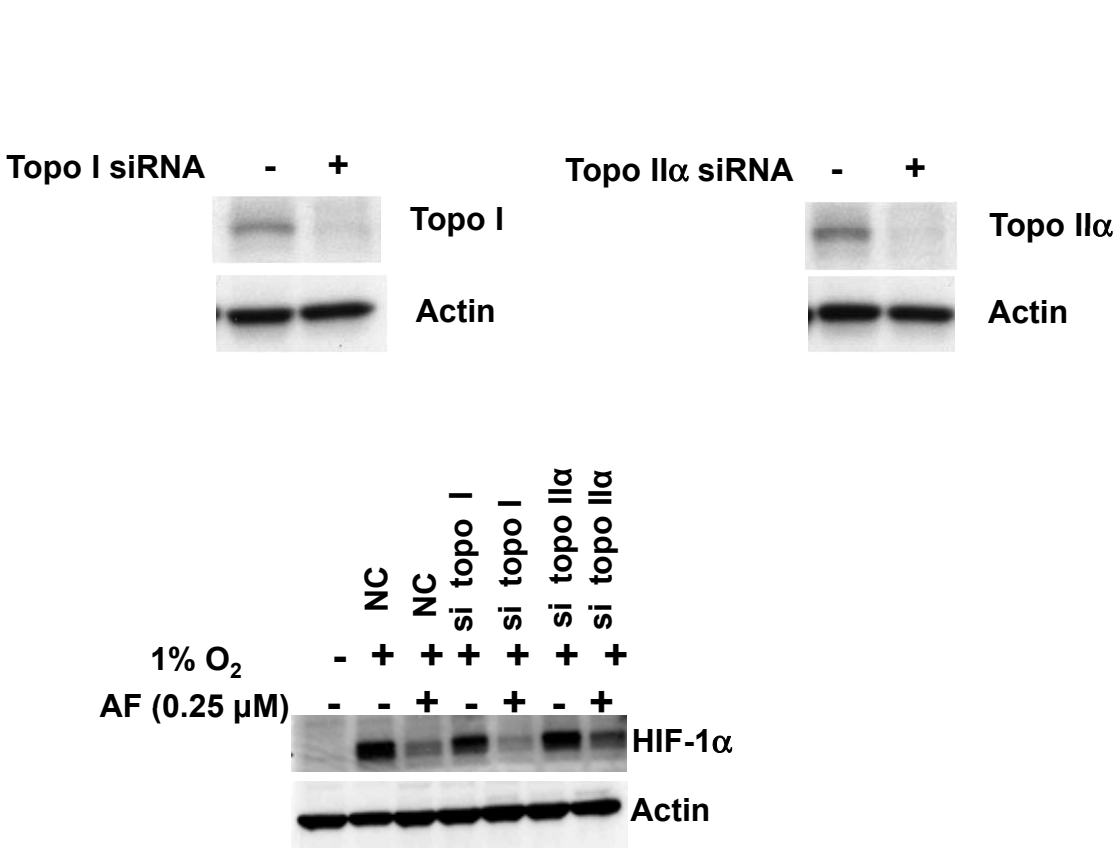

**Supplementary figure 1. AF does not inhibit HIF-1α protein expression in MDA-MB-231 cells.** MDA-MB-231 cells were cultured under normoxia or under hypoxic condition in the absence or presence of increasing concentrations of AF for 16 hours. Levels of HIF-1α and HIF-1β protein expression were analyzed by western blot.

# Supplementary Figure 2



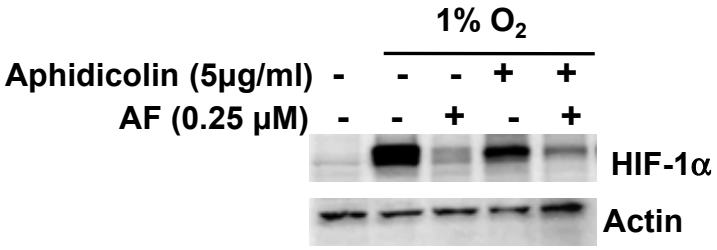

**AhR is not required for the inhibition of HIF-1α by AF.**
**A)** MCF7 cells were transfected with siRNA targeting SULT1A1or AhR, as described in Materials and Methods. Forty eight hours following transfection, SULT1A1 and AhR protein levels were analyzed by western blot. **B)** MCF7, transfected with siRNA targeting either SULT1A1 (siSULT1A1), AhR (siAhR) or negative control siRNA (NC), were treated for 16 hours in the presence or absence of AF (0.25 µM) under hypoxic conditions. HIF-1α and actin protein levels were analyzed by western blot. HIF-1α relative amount (obtained by densitometry, normalized by actin levels) is shown. Data are presented as fold change from hypoxic treated cells for each siRNA used.

## Supplementary Figure 3



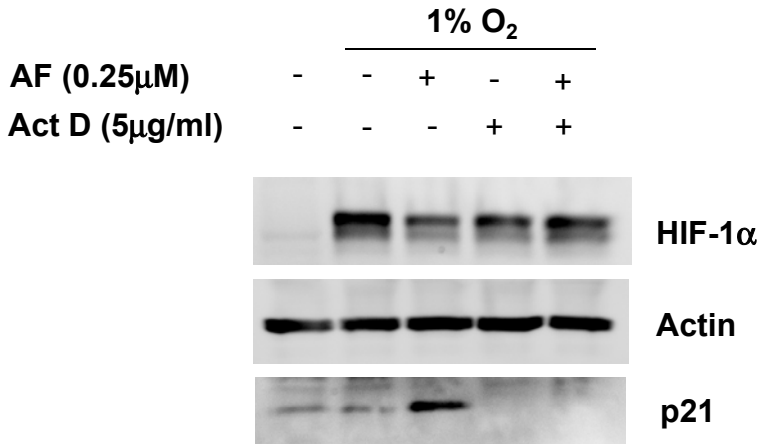

**AF inhibits HIF-1α protein accumulation in a topoisomerase independent manner.** **A)** MCF7 cells were transfected with siRNA targeting topo I or topo IIα (Dharmacon) as described in Materials and Methods. Topo I,Topo IIα and actin protein expression were analyzed by western blot. **B)** MCF7 cells transfected with siRNA targeting topo I or topo IIα and then cultured under normoxic or hypoxic conditions in the absence or presence of AF (0.25 μM) for 16 hours. HIF-1α and actin protein expression were analyzed by western blot.

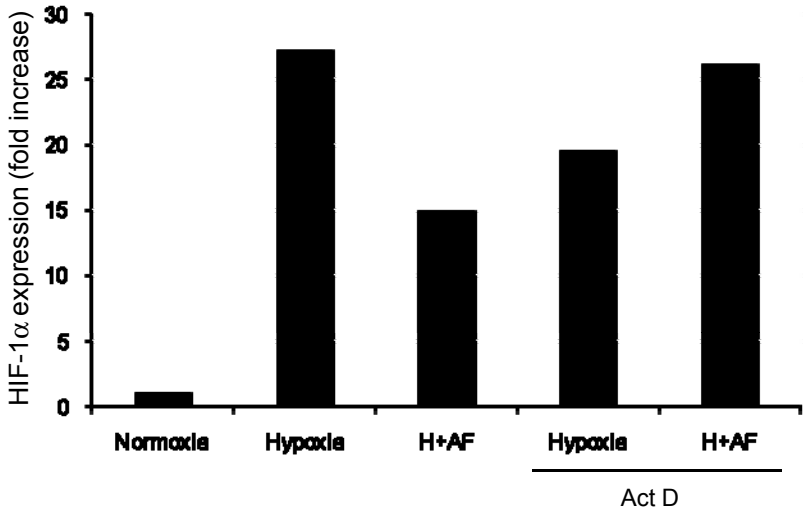
# Supplementary Figure 4




**Inhibition of HIF-1α protein accumulation by AF is DNA-replication independent.**
MCF-7 cells were cultured under normoxia or under hypoxia in the absence or presence of AF (0.25 μM) or aphidicolin (5μg/ml) for 16 hours. HIF-1α and actin protein levels were assessed.

# Supplementary Figure 5



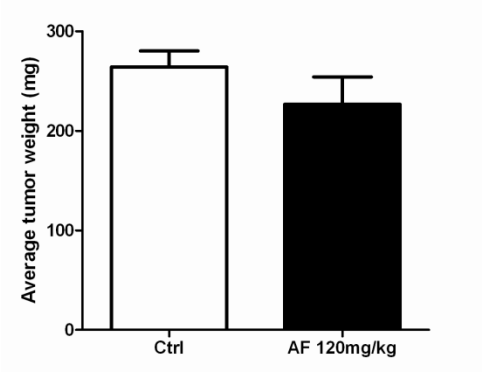




**Active transcription is required to inhibit HIF-1α protein accumulation by AF.**

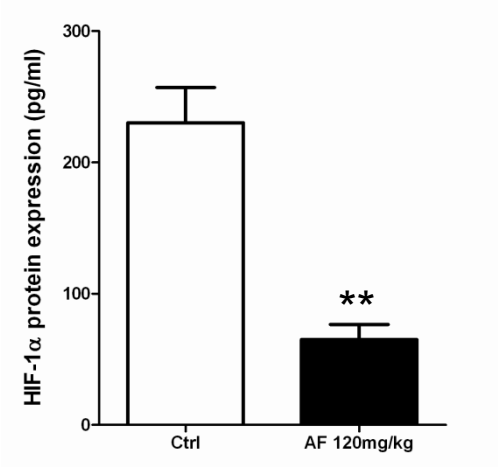
MCF-7 cells were cultured under normoxia or under hypoxia in the absence or presence of AF (0.25 μM) or Actinomycin D (5μg/ml) for 16 hours. HIF-1α, actin and p21 protein levels were assessed (top panel). HIF-1a protein levels were quantified , normalized by Actin and expressed as fold increase from normoxia (botton panel).

# Supplementary Figure 6

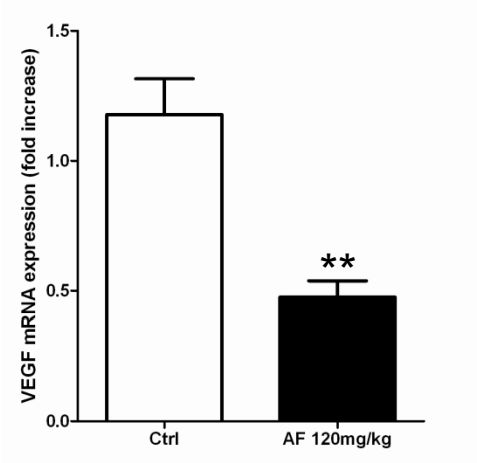
**A**




**B**




**C**




**AF inhibits HIF-1α in the absence of tumor growth inhibition in MCF7 xenografts.**

**A)** MCF-7 cells were implanted into nude mice (*n* = 4 per group) and allowed to grow up to ~ 200mg, when treatment was started daily for two days. On day 2, no significant reduction of tumor weight was observed in mice treated with AF, relative to vehicle-treated controls. **B)** Quantitative determination of HIF-1α using electrochemiluminescence assay as described in Material and Methods (**, $p < 0.05$). **C)** Expression of VEGF mRNA in tumor lysates from mice treated with vehicle or AF measured by real-time PCR. (**, $p < 0.05$).