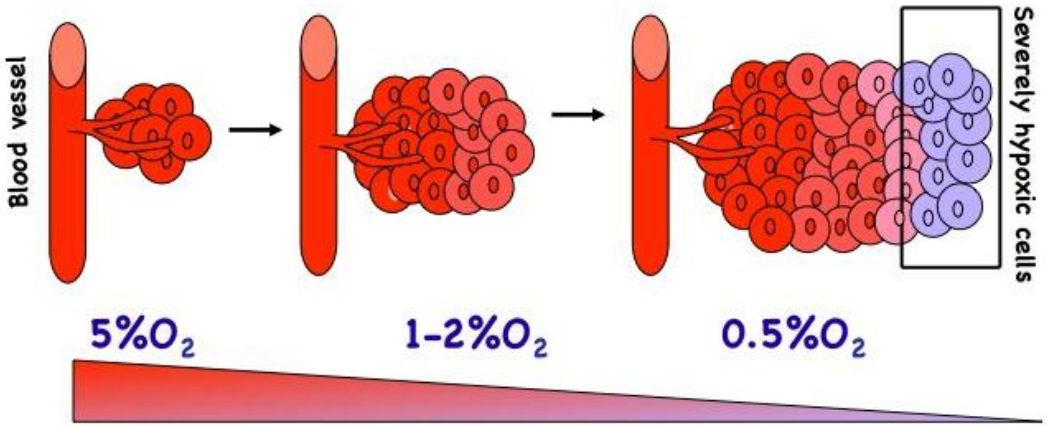
HYPOTHESIS

Gradients of O_2 control skeletal development and homeostasis by regulating the HIF pathway



HIF-1α (Hypoxia Inducible Factor)

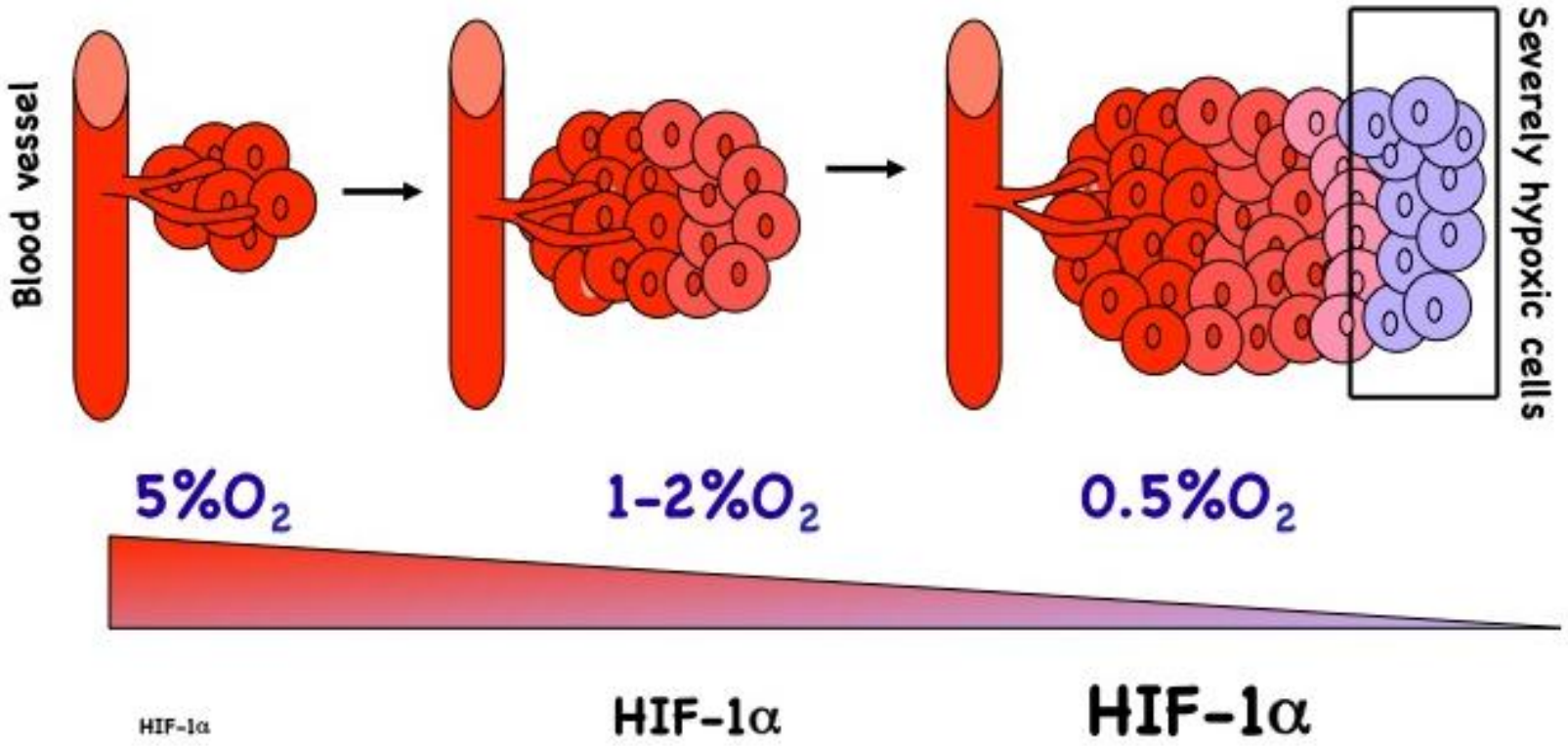
. PAS (PER-ARNT-SIM) subfamily of bHLH transcription factors

. heterodimer HIF-1α/ARNT; HIF-1α, the hypoxia -responsive component of the complex

. ubiquitously expressed and highly unstable

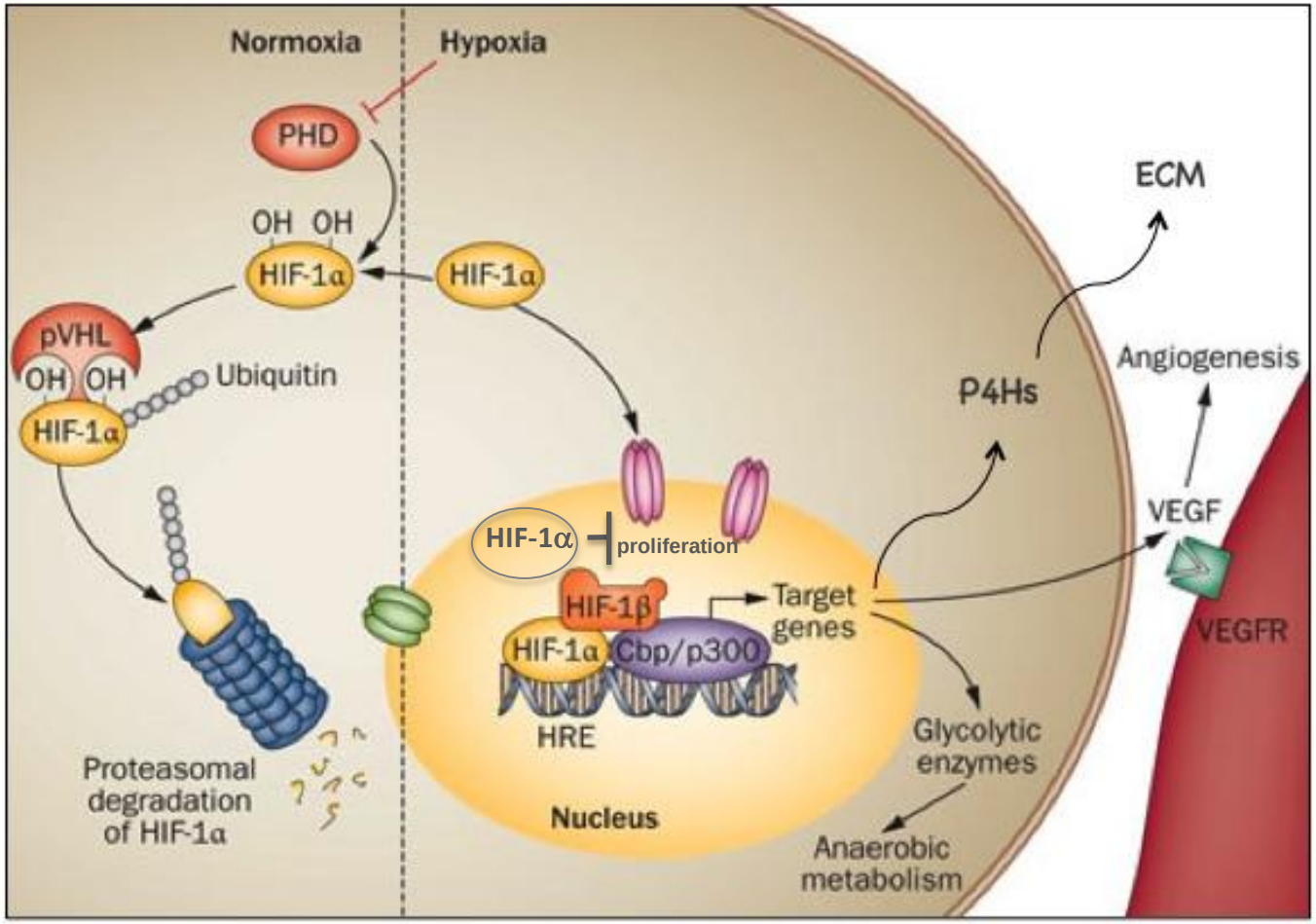
. *another member in the family, HIF-2α*

HIF-1α: A KEY FACTOR IN CELLULAR ADAPTATION TO HYPOXIA



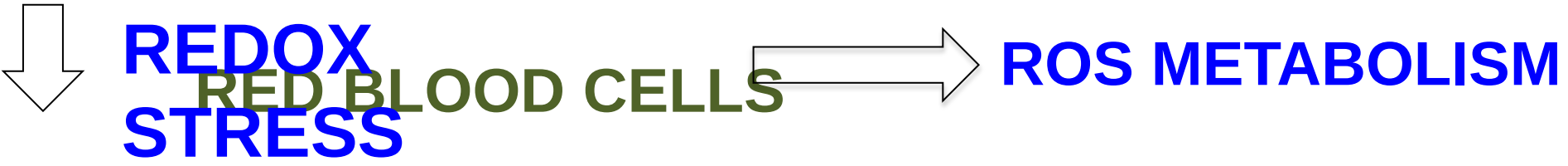
HIF-1α: A KEY MEDIATOR OF CELLULAR ADAPTATION TO HYPOXIA

In normoxia, HIF-1α protein is rapidly degraded by the proteosome



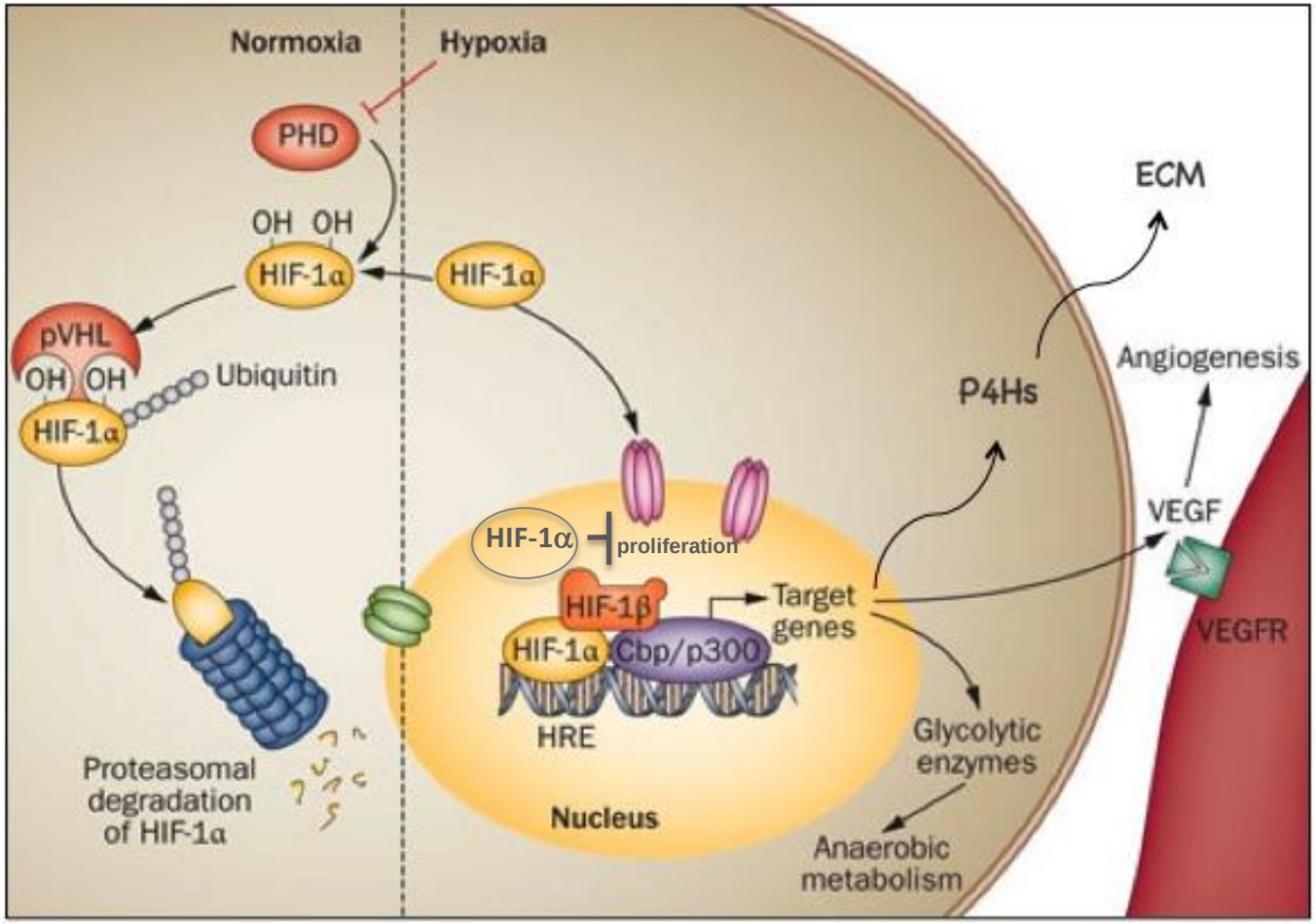
Modified from Nature Review Rheumatology 2012; 8:358-366

HIFs: A HOMEOSTATIC RESPONSE TO KEEP HYPOXIA "*IN CHECK*"



HYPOTHESIS

The complex actions of HIFs on O_2 homeostasis are exploited to modulate development and homeostasis of skeletal elements.



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