

Ernestina Schipani

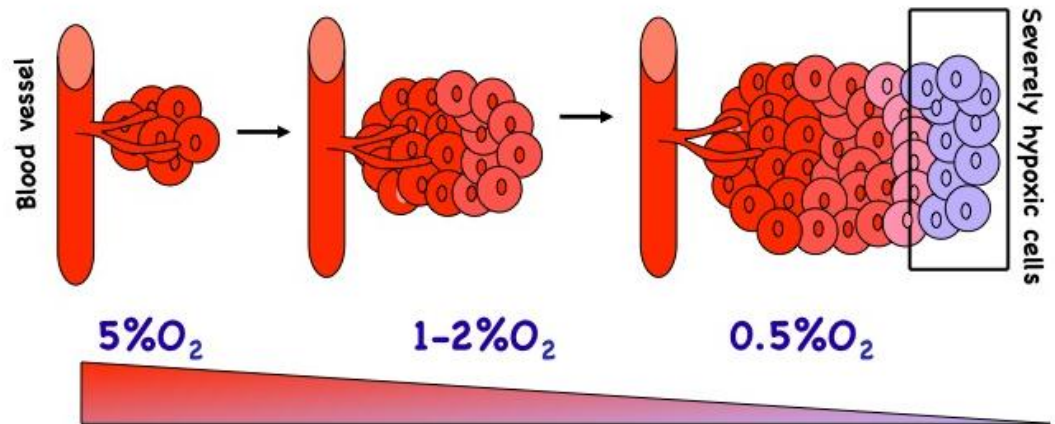
Associate Professor

MGH-Harvard Medical School

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HYPOTHESIS

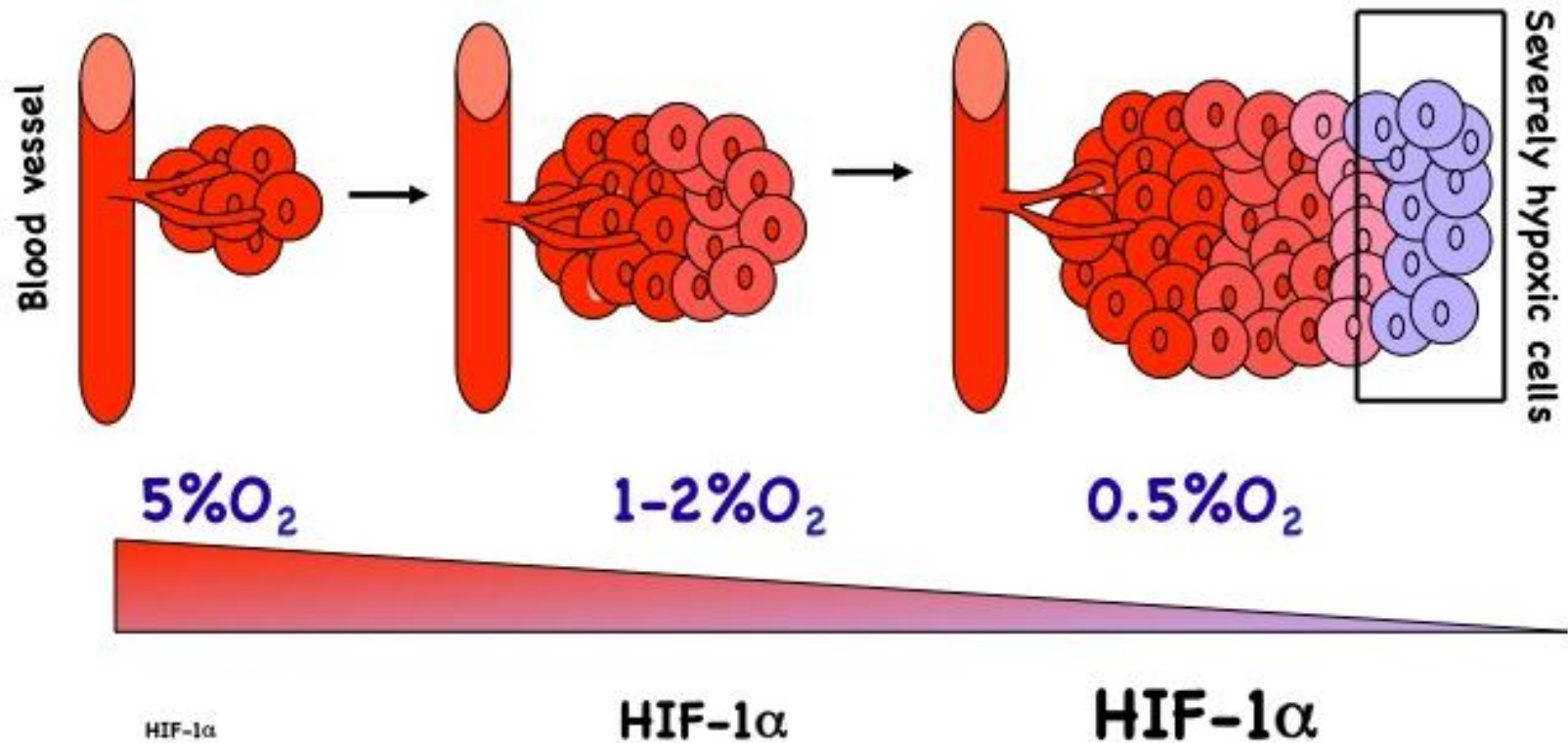
Gradients of O_2
control
skeletal
development
and homeostasis
by regulating
the HIF pathway



HIF-1 α (Hypoxia Inducible Factor)

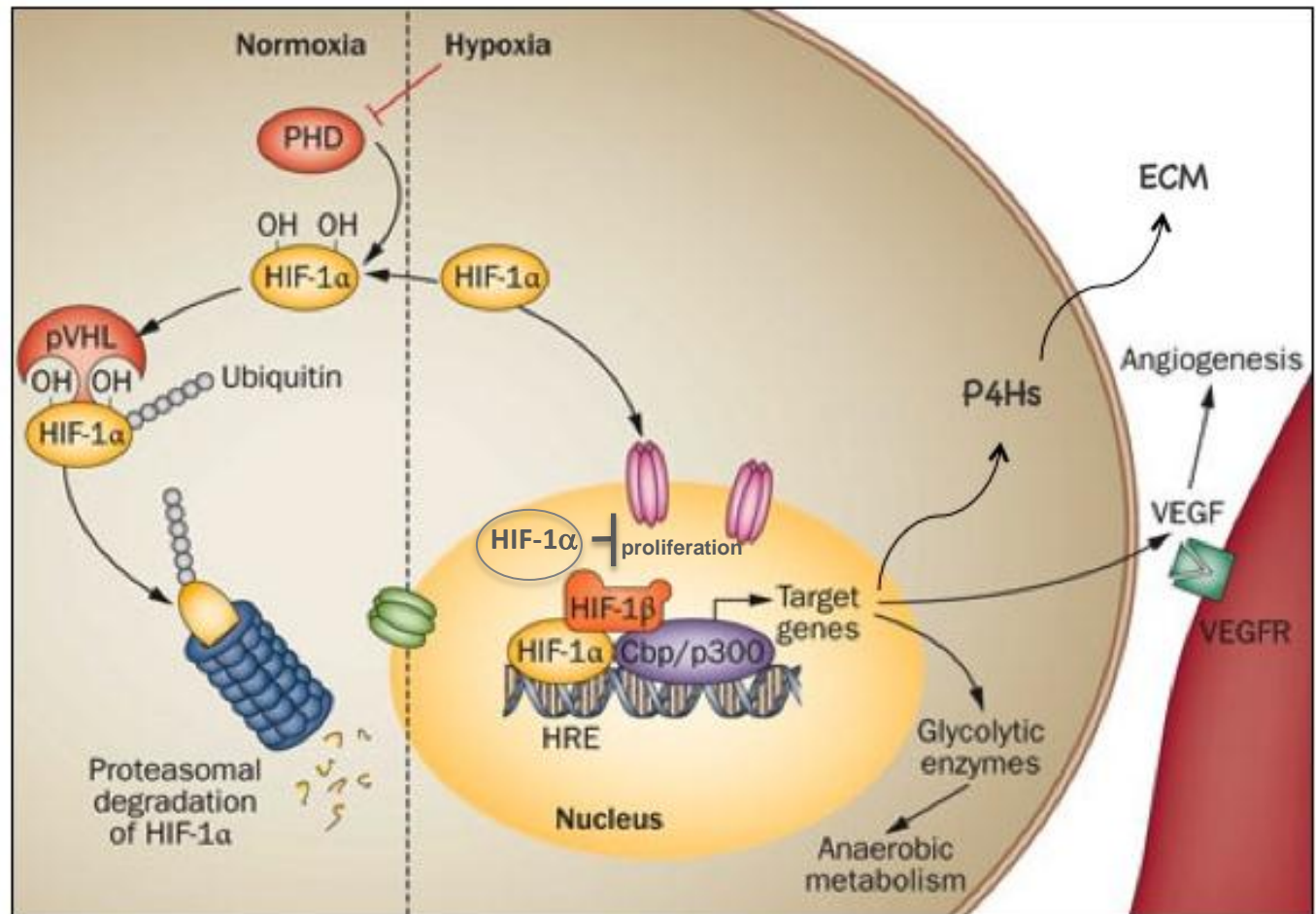
- . PAS (PER-ARNT-SIM) subfamily of bHLH transcription factors
- . heterodimer HIF-1 α /ARNT; HIF-1 α , the hypoxia -responsive component of the complex
- . ubiquitously expressed and highly unstable
- . *another member in the family, HIF-2 α*

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



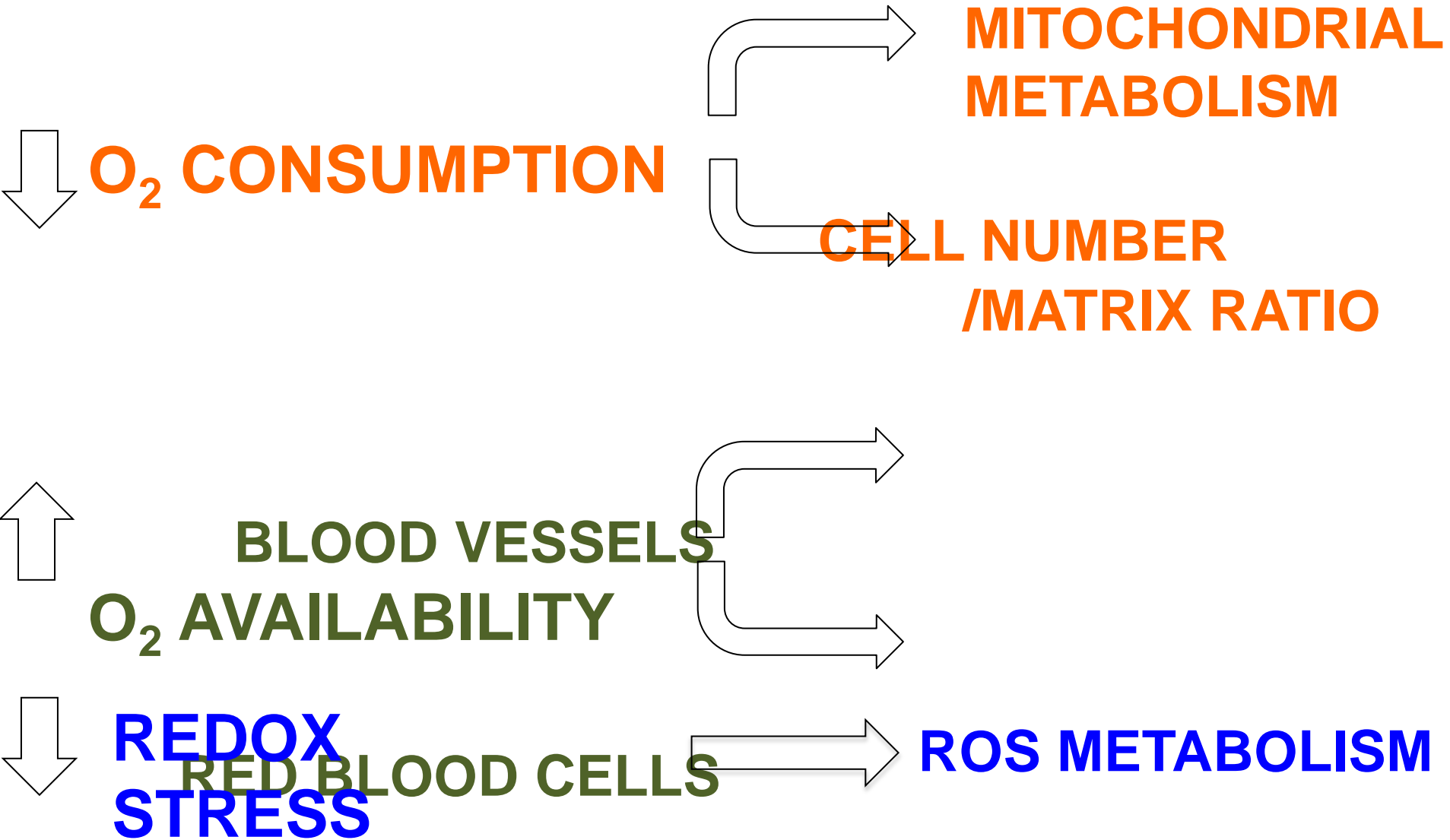
HIF-1 α : A KEY MEDIATOR OF CELLULAR ADAPTATION TO HYPOXIA

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



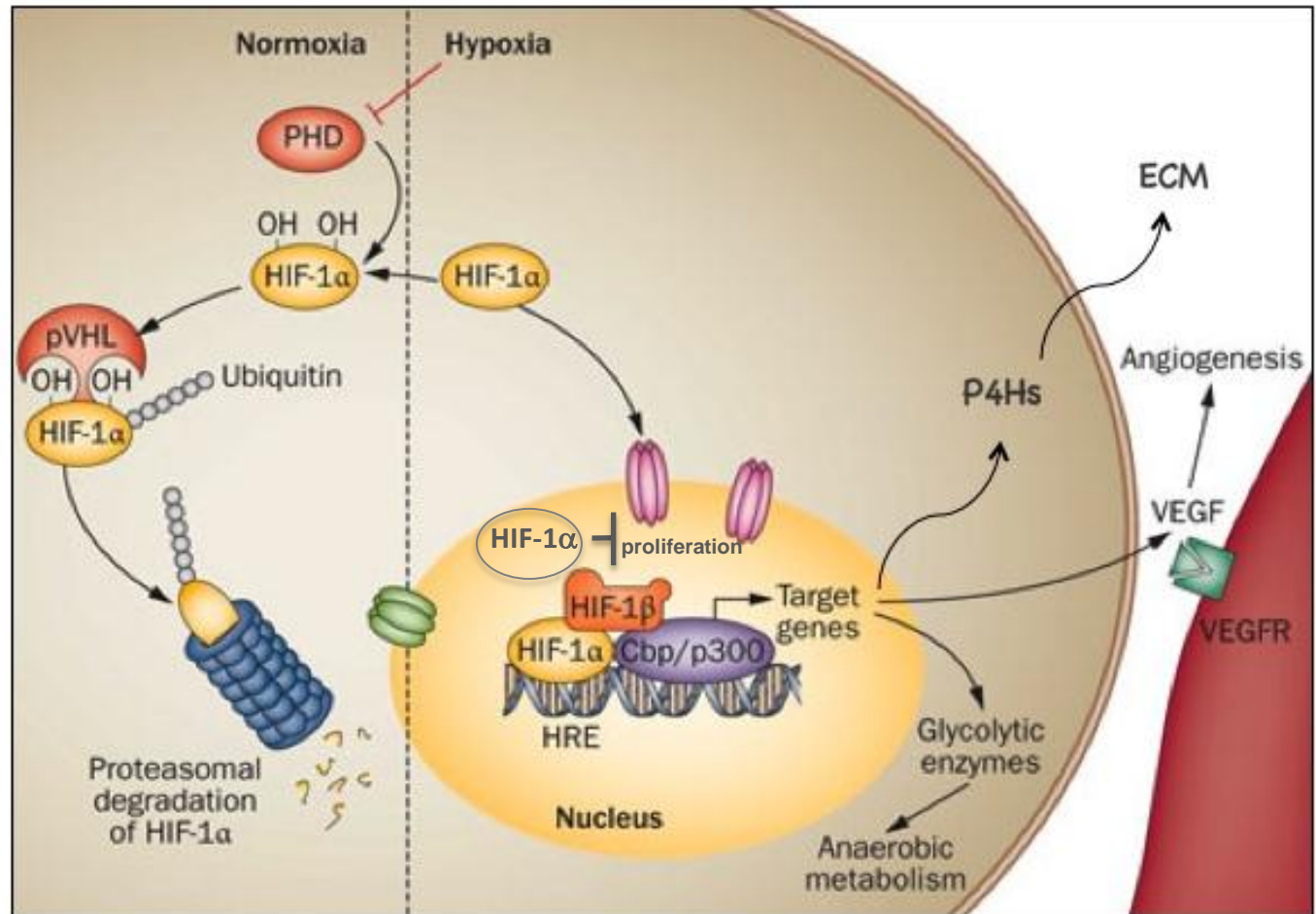
Modified from Nature Review Rheumatology 2012; 8:358-366

HIFs: A HOMEOSTATIC RESPONSE TO KEEP HYPOXIA “*IN CHECK*”



HYPOTHESIS

The complex actions of HIFs on O₂ homeostasis are exploited to modulate development and homeostasis of skeletal elements.



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