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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”

- O$_2$ CONSUMPTION
- MITOCHONDRIAL METABOLISM
- CELL NUMBER/MATRIX RATIO
- BLOOD VESSELS
- O$_2$ AVAILABILITY
- REDOX STRESS
- RED BLOOD CELLS
- ROS METABOLISM
HYPOTHESIS

The complex actions of HIFs on O$_2$ homeostasis are exploited to modulate development and homeostasis of skeletal elements.
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