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BAKER SCIENTIFIC APPLICATION NOTE

SCI-tive is a physiologically relevant, protected and controlled environment workstation for researchers that need a bit more space that can be, if desired, expanded to a multi-chamber GMP-level controlled system.

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Osteoarthritis

Why are O_2 levels in osteoarthritis studies important?

BACKGROUND

Osteoarthritis is characterised by loss of articular hyaline cartilage. Hyaline cartilage does not have blood vessels, therefore this environment is naturally devoid of oxygen and regulated by hypoxia.

- HIF-1 is ONLY active in low O_2 conditions
- HIF-1 regulates the homeostasis of cartilage tissue; chondrocytes do not survive or grow without HIF-1 activity (Pfander *et al*, Int Ortop, 2005)
- HIF-1 controls matrix synthesis and energy production of chondrocytes (Coimbra *et al,* Osteoarthitis Cartilage, 2004)
- T GF-β signaling needs hypoxia to enhance endoglin expression (Jahr et al Int J Mol Sci 2019)
- In ambient O_2 levels chondrocytes experience oxidative stress due to the increase of reactive oxygen species (ROS)

  → Increased NF-kB signaling and proinflammatory reactions (Chu *et al* Inflammation 2020)

  → Telomere instability and apoptosis induction

The SCI-tive range of advanced physiological oxygen workstations are designed to mimic *in vivo* conditions.

Scan the QR code to read more about the SCI-tive range!

TOPIC

Chondrocytes, osteoarthritis and oxygen

Articular cartilage damage has low healing potential due to the lack of vasculature and low cell density thus creating a challenge for orthopedic surgeons. Recently, new techniques have enabled regeneration of cartilage lesions and cartilage homeostasis. Untreated lesions can lead to osteoarthritis (1).

Articular cartilage in adults is avascular and their environment therefore is relatively hypoxic. Oxygen concentration can vary from 7% O_2 to 2% O_2 (as opposed to inhaled air at sea level containing approx. 21% O_2 (2,3,4). Different oxygen tensions influence many functions of chondrocytes including their metabolism, growth factor secretion, proteoglycan synthesis, etc. (6). A vast body of data supports the notion that optimal physiological conditions for maintaining chondrocyte homeostasis, proper phenotype, and metabolism of these cells *in vitro* is ideally between 2-5% O_2 (7,8).

Hypoxia Inducible Factor (HIF) is a transcription factor that governs most cellular responses to oxygen. It gets stabilized and active in varying O_2 levels around and below 5% O_2.

Its function is essential for the normal, biologically relevant function of tissues and cells. In cartilage, HIF is relatively highly expressed and the HIF-1 isoform has been shown to be of great importance in promoting matrix accumulation, decreasing degradation and hypertrophy (8).

Local activation of HIF-1 is also necessary for chondrocyte survival in the center of the expanding growth plate albeit in a controlled fashion (10-14).

TFG-β superfamily signaling is important in articular chondrocytes for their development and homeostasis. This superfamily also includes bone morphogenetic proteins (BMPs). HIF-1 promotes TGF-β Smad signaling in hypoxia. TGF-β signaling pathway is critical for chondrocytes, MSCs and synovial lining cells during OA development and progression, as this signaling drives chondrocytes toward hypertrophy, promoting osteoprogenitor cell differentiation into osteoblasts and angiogenesis in subchondral bone, and stimulating synovial lining cells expansion and fibrosis (15).

SUMMARY

In summary, the *in vivo* environment of chondrocytes is always low in oxygen. This is an environment chondrocytes are conditioned to need in order to survive.

In order to conduct research and develop regenerative medicine for osteoarthiritis study conditions have mimicked these conditions in order to support biologically correct cellular signaling in chondrocytes.

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