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Maintaining physiological fidelity during *in vitro* stem cell culture and expansion; a role for oxygen control

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Hypoxia or physiological normoxia, plays a key role in determining stem cell behaviour in the *in vivo* niche. In spite of this little attention is payed to the role of reduced oxygen levels during *in vitro* culture generating a risk of forced paradigm and artefactual norms. Bone marrow-derived human mesenchymal stem cells (hMSC), due to the sinusoidal blood vessel architecture found within their niche, are particularly vulnerable to oxygen tension fluctuations. We and others, have now described fundamental, artefactual, alterations in hMSC biology as a consequence of air oxygen exposure. These include reduced colony forming unit-fibroblastic isolation; dysregulated epigenome, transcriptome and proteome; altered biochemical volatile footprints during culture; and counter intuitive alterations in reactive oxygen species management. This lecture will discuss the fundamental biology underpinning these biological differences, their potential impact on regenerative medicine and what we can do to transform biological understanding into therapeutic application.

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