Relevance of Oxygen Concentration in Stem Cell Culture for Regenerative Medicine

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SUMMARY

- Oxygen plays a significant role in stem cell growth.
- Stem cells are commonly grown in atmospheric oxygen conditions (21%) but this is not ideal for preserving their desired stemness when producing ATMPs.
- Culturing cells under natural physiological oxygen levels (physioxia) results in increased proliferation, migration, and angiogenesis, along with reduced senescence and apoptosis.

POINTS OF EMPHASIS

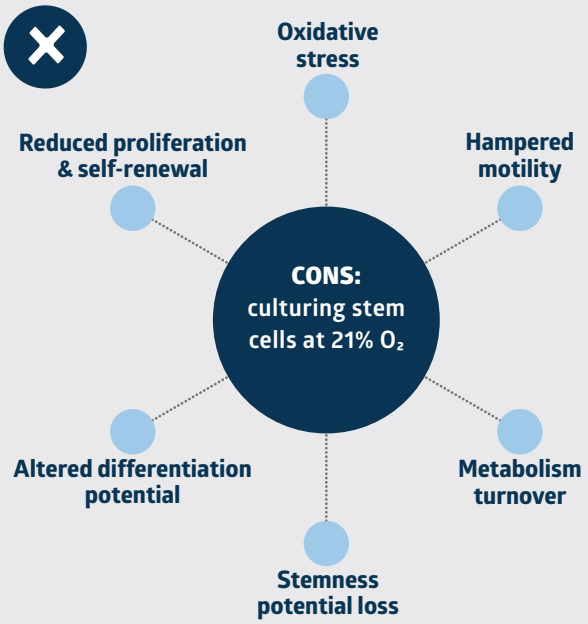
- Importance is given to balancing nutrients, growth factors and pH buffers for cell growth cells in vitro.
- Poor emphasis is given to oxygen concentrations in culture media for optimal growth.
- Standard environmental O2 levels (21%) create a hyperoxic environment that can impair stem cell behaviour.

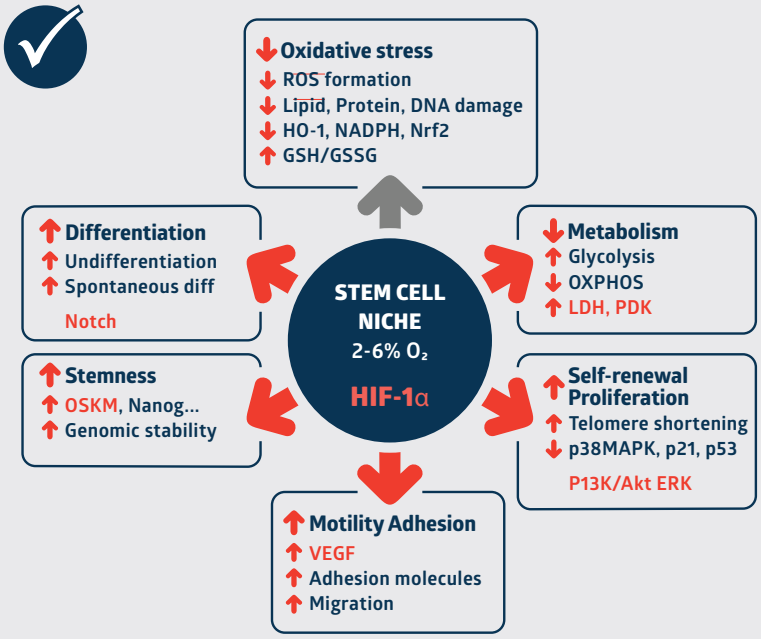
PO_2%	HUMAN ORGANS
1%	**Eye:** 1.0 – 5.0% **/ Bone/Cartilage:** 1.4%
2%	**Heart:** 2.0 – 6.0% **/ Uterus:** 2.5% **/ Pancreas:** 2.7 – 6.0% **/ Small Intestine (Lumen):** 2.0 – 5.0%
3%	**Skin (subcutaneous level):** 3.0 – 8.0% **/ Brain:** 3.0 – 5.0% **/ Muscle Fiber:** 3.0 – 10.0%
4%	**Kidney:** 4.0 – 9.5% **/ Liver:** 4.0 – 7.0% **/ Dental Pulp:** 4.0%
5%	**Bone Marrow:** 5.4 – 7.0% (has been seen as low as 1.5%)
6%	**Stomach:** 6.0 – 10.0%
7%	
8%	
9%	
10%	
11%	
12%	**Blood Vessels:** 12.0%
13%	**Lungs + Alveoli:** 13.0 – 14.0%
14%	

CONCLUSION: Oxygen concentration is an essential factor when culturing stem cells for ATMPs and regenerative medicines.

REFERENCE

Mas-Bargues, C., Sanz-Ros, J., Román-Domínguez, A., Inglés, M., Gimeno-Mallench, L., El Alami, M., Borrás, C. (2019). Relevance of Oxygen Concentration in Stem Cell Culture for Regenerative Medicine. *International Journal of Molecular Sciences*, 20(1195), 1-27. Retrieved from https://doi.org/10.3390/ijms20051195





Stem cells cultured at 21% O_2 do not preserve the desired stemness when producing ATMPs.

The effects of culturing stem cells between 2 - 6% O_2. Red arrows indicate which cell functions HIF-1a influences. HIF-1a is expressed under lower O_2.

6 KEY CELL ELEMENTS AFFECTED BY O_2:

1. Reactive Oxygen Species (ROS) Formation:

i. Low levels of ROS are required by stem cells to maintain quiescence and self-renewal.

2. Metabolism:

i. Stem cells typically rely on glycolysis (oxygen independent).

ii. Stem cells grown in most incubators, BSCs, and isolators (21% O2) are forced to switch to oxygen consumption by OXPHOS and decrease their glycolysis.

iii. This metabolic switch increases:

a. Senescence.

b. oxidative damage.

c. genomic instability.

d. decreased lifespans.

3. Self-Renewal and Proliferation Rate:

i. Studies have observed low proliferation rates at environmental oxygen tension compared to physiological niches in many stem cell types.

4. Differentiation Fate:

i. Low oxygen tensions keep human stem cells in a self-renewable undifferentiated state.

5. Stemness Maintenance:

i. Low oxygen tension promotes the undifferentiated state in several stem cell types through various genetic controls.

6. Reprogramming Efficiency:

i. Oxygen is a key factor that affects reprogramming efficiency.

ii. Reprogramming to pluripotency requires a shift from oxidative to glycolytic metabolism.

iii. This shift is mediated by HIF1α and HIF2α, two factors induced by low oxygen tensions.

Learn more about the Whitley GMP Oxygen-Controlled Isolator

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