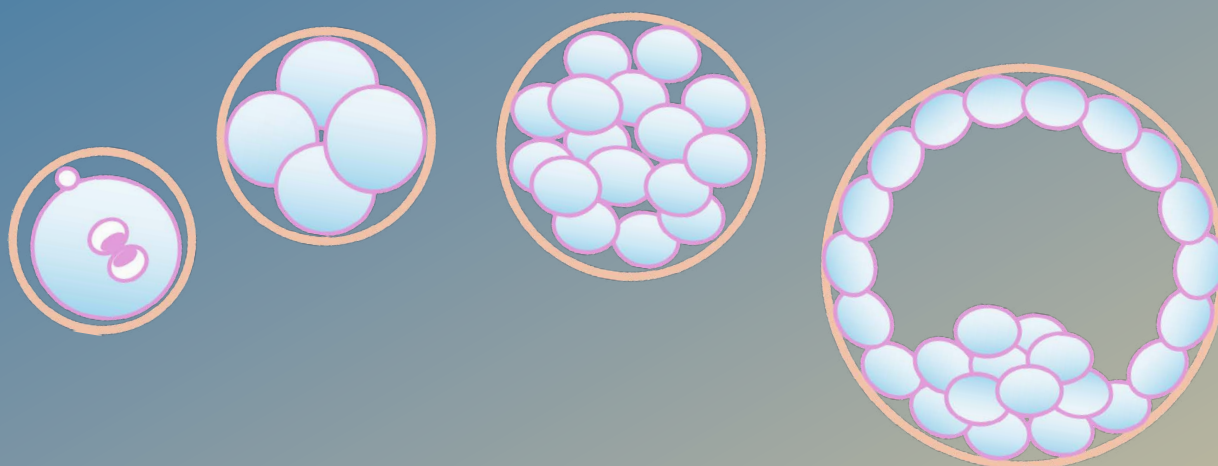




Technical Note

Optimizing *In Vitro* Fertilization Outcomes: The Role of Low Oxygen Conditions in Embryo Culture



Embrient Inc

Formerly known as



Tel: (858) 535-0545

Toll-Free: (877) 755-3309

Email: info@embrient.com

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Introduction

In vitro fertilization (IVF) has revolutionized assisted reproductive technologies, offering hope to many couples facing infertility, as well as serving as an essential reproductive technology for livestock and conservation biology to enhance breeding efficiency, preserve genetic diversity, and assist in the propagation of endangered species. A critical factor influencing the success of IVF is the culture environment of embryos, particularly oxygen concentration. *In vivo*, embryos develop in a low-oxygen (hypoxic) environment, with oxygen tensions ranging from 2% to 8% in the female reproductive tract. Contrastingly, standard IVF laboratory conditions often expose embryos to atmospheric oxygen levels (~20%), which may not be optimal for embryonic development.

Physiological Rationale for Low Oxygen in Embryo Culture

Embryos cultured under atmospheric oxygen concentrations are subjected to higher levels of reactive oxygen species (ROS), leading to oxidative stress, DNA damage, and impaired development. Culturing embryos under reduced oxygen tensions (5% O₂) more closely mimics the *in vivo* environment, potentially enhancing embryo quality and developmental competence.

Mechanisms Underpinning Improved Outcomes

The beneficial effects of low oxygen culture are attributed to:

- **Reduced Oxidative Stress:** Lower oxygen levels decrease ROS production, minimizing cellular damage.
- **Enhanced Gene Expression:** Hypoxic conditions influence gene expression patterns favorable for embryo development, mediated by the increased function of the transcription factor HIF-1.
- **Improved Metabolic Function:** Embryos cultured under low oxygen exhibit metabolic profiles more akin to *in vivo* conditions, promoting better developmental outcomes.

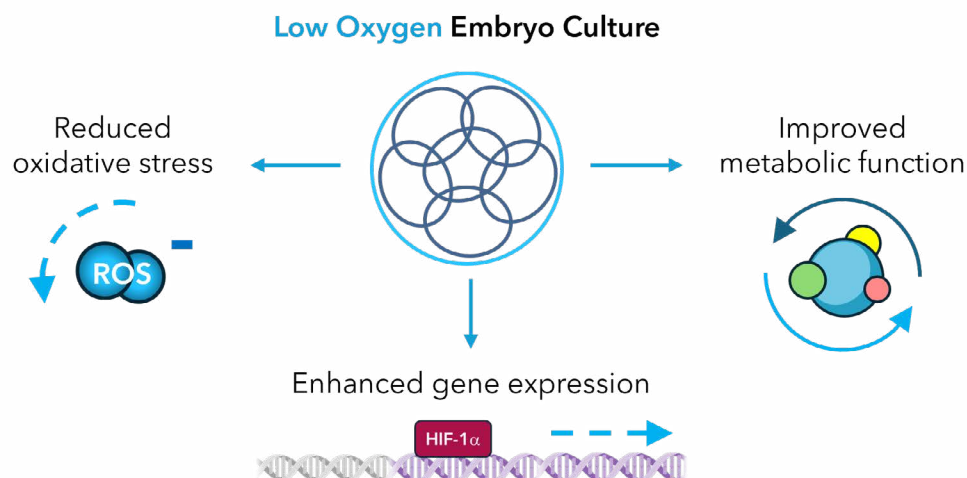


Fig. 1. Summary of the mechanisms by which low oxygen conditions enhance embryo development.

Clinical Evidence Supporting Low Oxygen Culture

Recent studies have investigated the impact of low oxygen conditions on IVF outcomes:

- **Embryo Development:** Konstantogianni *et al.* (2024) summarized studies reporting that embryos cultured under 5% O₂ exhibited improved blastocyst formation rates and higher quality embryos compared to those cultured under atmospheric oxygen levels.

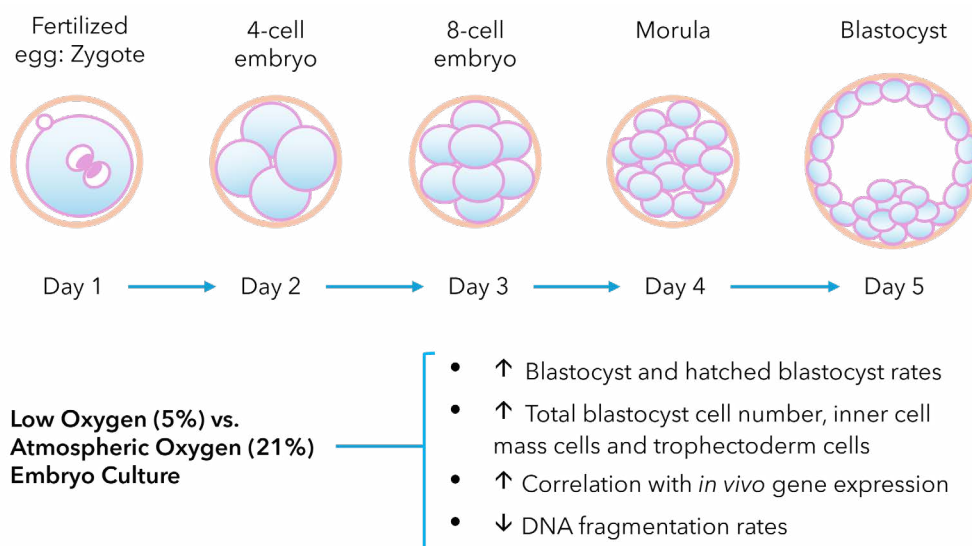


Fig. 2. The impact of oxygen concentration on blastocyst formation *in vitro*.

- **Pregnancy Rates:** A meta-analysis by Bontekoe *et al.* (2012) demonstrated that low oxygen culture conditions significantly increased clinical pregnancy rates, with an odds ratio (OR) of 1.39 (95% CI: 1.11–1.76), suggesting a 39% improvement over atmospheric conditions.
- **Live Birth Rates:** The same meta-analysis indicated that low oxygen culture could enhance live birth rates, with clinics potentially increasing success rates from 30% to between 32% and 43% by adopting reduced oxygen tensions.

Implementation in IVF Laboratories

To achieve low oxygen conditions:

- **Tri-Gas Incubators:** Utilize incubators capable of maintaining 5% O₂, 5% CO₂, and 90% N₂ environments. Embrient's [Modular Incubator Chamber](#) provides a low-cost, simple to use solution that uses far less gas than continuous flow incubators.

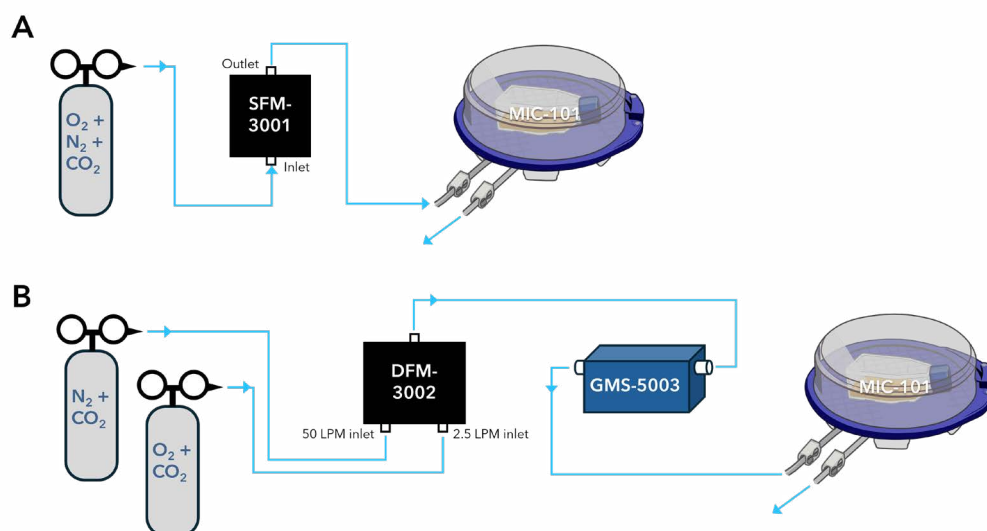


Fig. 3. Two possible setup configurations for the Modular Incubator Chamber, using either a pre-mixed tri-gas mixture or a less costly dual gas mixture that is mixed in real-time. SFM-3001; Single Flow Meter, DFM-3002; Dual Flow Meter, GMS-5003; Gas Mixing System, MIC-101; Modular Incubator Chamber. Components are attached using PVC tubing, TUB-516. These setup components are available as [product bundles](#).

- **Gas Supply:** Ensure a consistent supply of appropriate gas mixtures, with regular monitoring and calibration. As described above, premixed tri-gas mixtures are simpler to use, but are typically more expensive, while dual gas sources provide a lower cost option.
- **Culture Media:** Use media formulations optimized for low oxygen conditions, potentially supplemented with antioxidants to further mitigate oxidative stress.

Considerations and Challenges

While the benefits of low oxygen culture are evident, laboratories must consider:

- **Cost Implications:** Opting for full sized, continuous flow, low oxygen incubators may be required for large scale tissue culture but comes at a high price. Embrient's Modular Incubator Chamber enables researchers to get quickly up to speed with low oxygen environments, while keeping costs low. There are additional advantages of the Modular Incubator Chamber over conventional CO2 incubators discussed in this tech note.
- **Protocol Standardization:** Establishing consistent protocols is essential to maximize benefits and ensure reproducibility.
- **Training:** Staff should be adequately trained in handling and maintaining low oxygen culture systems.

Conclusion

Adopting low oxygen conditions in embryo culture aligns IVF practices more closely with physiological conditions, offering tangible benefits in embryo quality and clinical outcomes. As evidence mounts supporting its efficacy, integrating low oxygen culture into standard IVF protocols represents a promising advancement in reproductive medicine.

References

1. Konstantogianni O, Panou T, Zikopoulos A, Skentou C, Stavros S, Asimakopoulos B. Culture of Human Embryos at High and Low Oxygen Levels. *J Clin Med*. 2024 Apr 11;13(8):2222. doi: 10.3390/jcm13082222. PMID: 38673495; PMCID: PMC11050882.
2. Bontekoe S, Mantikou E, van Wely M, Seshadri S, Repping S, Mastenbroek S. Low oxygen concentrations for embryo culture in assisted reproductive technologies. *Cochrane Database Syst Rev*. 2012 Jul 11;2012(7):CD008950. doi: 10.1002/14651858.CD008950.pub2. PMID: 22786519; PMCID: PMC11683526.