Journal of Fertilization: In Vitro - IVF-Worldwide, Reproductive Medicine, Genetics & Stem Cell Biology

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Perspective

Altered Telomere Dynamics in Human Embryos Cultured under Variable Oxygen Concentrations

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DESCRIPTION

Telomeres are repetitive nucleotide structures located at chromosome ends that preserve genomic stability during cellular division. These regions function as protective caps that prevent chromosomal fusion, degradation, and abnormal recombination. During each cell cycle, telomeres gradually shorten because conventional Deoxyribonucleic Acid (DNA) replication cannot fully duplicate terminal chromosome sequences. In reproductive biology, telomere maintenance has attracted increasing scientific attention due to its relationship with gamete quality, embryonic development, and long-term cellular viability. Within assisted reproductive laboratories, environmental conditions surrounding embryo culture may influence telomere stability during early developmental stages, particularly oxygen concentration during *in vitro* incubation.

Embryos generated through assisted reproduction are commonly cultured for several days before transfer or cryopreservation. During this interval, cleavage-stage embryos and blastocysts undergo rapid cellular division accompanied by extensive genetic activation. These developmental processes require stable DNA replication and balanced oxidative metabolism. Since telomeres are sensitive to oxidative stress, laboratory conditions that alter reactive oxygen species production may affect telomere dynamics within developing embryos.

Historically, many embryology laboratories cultured embryos under atmospheric oxygen concentrations approaching twenty percent. However, physiologic oxygen levels within the female reproductive tract are substantially lower, typically ranging between two and eight percent depending on anatomical location. Recognition of this difference encouraged adoption of reduced oxygen incubation systems designed to mimic natural reproductive conditions more closely. Several studies have reported improved blastocyst development and implantation rates when embryos are cultured under lower oxygen tension. Researchers have therefore examined whether reduced oxygen exposure also contributes to preservation of telomere integrity. Oxidative stress represents one of the principal mechanisms involved in telomere shortening. Reactive oxygen species can damage guanine-rich telomeric sequences, impair DNA replication, and activate cellular stress pathways. In early embryos, excessive oxidative injury may interfere with chromosomal stability and developmental competence. Laboratory-generated oxidative stress may arise from oxygen concentration, light exposure, fluctuations in temperature, or metabolic byproducts accumulating within culture media. Since telomeric DNA is particularly vulnerable to oxidative damage, embryo culture conditions may directly influence telomere length during preimplantation development.

Experimental investigations involving mammalian embryos have demonstrated measurable differences in telomere maintenance under varying oxygen conditions. Mouse embryos cultured in reduced oxygen environments often exhibit lower oxidative stress markers and improved cellular proliferation compared with embryos maintained at atmospheric oxygen levels. Some studies have also identified altered expression of telomerase-related genes under different incubation conditions. Telomerase is an enzyme complex responsible for adding telomeric repeats during cellular division, thereby supporting chromosomal stability. Although telomerase activity naturally occurs during early embryogenesis, environmental stress may influence its regulation.

Human embryo studies remain more limited because ethical and regulatory considerations restrict experimental manipulation. Nevertheless, indirect observations from surplus donated embryos and blastocyst analysis have provided useful information. Some reports indicate that embryos cultured under lower oxygen conditions display improved morphological quality and reduced apoptotic activity. Researchers have proposed that preservation of telomere stability may partly explain these findings, though direct causal relationships remain difficult to establish. Parental factors also contribute significantly to embryonic telomere dynamics. Maternal age is associated with reduced oocyte quality, mitochondrial dysfunction, and increased chromosomal abnormalities. Oocytes from older women may possess shortened telomeres before fertilization occurs. Similarly, paternal age and male infertility have been associated with altered sperm telomere characteristics. Since

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Received: 01-Sep-2025, Manuscript No. JFIV-25-41832; **Editor assigned:** 03-Sep-2025, PreQC No. JFIV-25-41832 (PQ); **Reviewed:** 17-Sep-2025, QC No. JFIV-25-41832; **Revised:** 24-Sep-2025, Manuscript No. JFIV-25-41832 (R); **Published:** 01-Oct-2025, DOI: 10.35841/2375-4508.25.13.426

Citation: Ortega C (2025). Altered Telomere Dynamics in Human Embryos Cultured under Variable Oxygen Concentrations. J Fertil *In Vitro* IVF World w Reprod Med Gent Stem Cell Biol. 13:426.

embryos inherit telomeric material from both gametes, baseline parental factors interact with laboratory conditions during development.

Mitochondrial activity plays a central role in this relationship. Mitochondria generate energy required for embryonic division but also produce reactive oxygen species as metabolic byproducts. Excess oxidative stress may impair both mitochondrial and nuclear DNA integrity. Reduced oxygen culture systems appear to support more balanced mitochondrial metabolism in some embryo studies, potentially decreasing telomere damage during cleavage and blastocyst formation. Researchers continue to investigate how metabolic regulation and telomere maintenance interact during preimplantation development. Culture media composition may further influence telomere stability. Amino acid concentration, antioxidant supplements, glucose availability, and potential of Hydrogen (pH) balance all affect cellular metabolism during embryo culture. Some media formulations include antioxidants designed to reduce oxidative injury. Compounds such as taurine, glutathione, and pyruvate may help neutralize reactive oxygen species within the culture environment. Although evidence remains incomplete, optimized media composition may contribute to preservation of chromosomal stability during embryogenesis.

Time-lapse embryo monitoring systems have introduced additional opportunities for evaluating developmental patterns under different oxygen conditions. These incubators permit continuous embryo observation without repeated removal from controlled environmental settings. Reduced handling may minimize temperature and gas fluctuations that contribute to oxidative stress. Some embryologists have observed more synchronized cleavage patterns and improved blastocyst expansion when embryos remain within stable low-oxygen culture systems throughout development. As reproductive technologies continue to evolve, understanding cellular responses to laboratory environments remains essential. Telomeres provide an important indicator of chromosomal health during rapid embryonic division. Current evidence suggests that oxygen concentration influences oxidative stress and may affect telomere stability during preimplantation culture. Further research combining molecular genetics, embryology, and developmental biology may contribute to safer laboratory protocols and improved reproductive outcomes for patients undergoing assisted conception procedures.

CONCLUSION

As reproductive technologies continue to evolve, understanding cellular responses to laboratory environments remains essential. Telomeres provide an important indicator of chromosomal health during rapid embryonic division. Current evidence suggests that oxygen concentration influences oxidative stress and may affect telomere stability during preimplantation culture. Further research combining molecular genetics, embryology, and developmental biology may contribute to safer laboratory protocols and improved reproductive outcomes for patients undergoing assisted conception procedures.